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JPRS L/9591

5 March 1981

... FBIS 40TH YEAR 1941-81 ...

USSR Report

BIOMEDICAL AND BEHAVIORAL SCIENCES

(FOUO 6/81)



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On behalf of all of us in FBIS I wish to express appreciation to our readers who have guided our efforts throughout the years.

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USSR REPORT
LIFE SCIENCES
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ADVANCED BIOTECHNOLOGY

UDC 632.9.3.2.2.

MODERN TRENDS IN THE USE OF BIOLOGICAL ACTIVE SUBSTANCES AS
PLANT PROTECTION AGENTS

Moscow BIOLOGICHESKI AKTIVNYYE VESHCHESTVA V ZASHCHITE RASTENIY
in Russian 1979 pp 3-9

[Article by Ye. M. Shumakov, doctor of biological sciences, professor, All-Union
Scientific-Research Institute for Protection of Plants]

[Text] In the past three to five years (1974-1978), new plant protection agents
have enjoyed practical application both in the USSR and abroad, chief among
these being insect pheromones and hormonal compounds.

This has been the result of intensive scientific research efforts carried out by
entomologists in cooperation with animal physiologists and chemists studying the
structure of natural compounds.

In April, 1976, at the Scientific and Technical Council of the USSR Ministry of
Agriculture (MSKh SSSR), the question of the state of the art and the outlook
of pheromone use to control crop pests was discussed. One of the decisions of
this council emphasized the need for wide-scale comparative testing of domestic
and imported pheromones.

The results of these tests for 1976 were summarized at a special session at the
VDNKh in February, 1977.

The Institute of Zoology and Parasitology of the Lithuanian Academy of Sciences
held two all-union symposia on insect chemoreceptors in Vilnius and published the
proceedings of these symposia ("Khemoretseptsiya nasekomykh", Vilnius, I, 1971;
II, 1975; III, 1978). A third symposium is now in the planning stage.

Of late, not a single meeting has been held in our country on the subject of
endocrinology. In this respect, we have had valuable contacts and cooperative
ventures with scientists at the Czechoslovak Academy of Sciences, where
wide-scale investigation of endocrinological problems in insects in both their
biological and chemical aspects is being carried out.

At special symposia of the 15th International Entomological Congress (Washing-
ton, 1976), attention was sharply focused on the study of biologically active

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substances which ensure the development of insects and chemical communications among individual organisms. Most scientists tend to accept a division of biologically active substances into two categories: hormones and semiotic chemicals. The latter imply chemical messengers which govern chemical interaction among organisms and in some way affect their social and sexual behavior.

In line with this categorization, two basic trends have developed in the study of means to employ biologically active substances in plant protection.

One trend involves the study of new methods to control pests based on the use of substances which inhibit or suppress growth, development and reproduction of insects. Among these are the juvenoids, hormonal compounds which inhibit molting and incorporation of chitin in the insect cuticle, such as the new drug Dimilin® [difluron]; substances which inhibit diapause, chemosterilants, etc.

Another trend in the use of biological active substances as plant protection agents is based on the use of drugs which affect the social and sexual behavior of insects and in some way affects the ecology.

This category primarily includes various types of pheromones, e.g. sexual, trail, territorial and alarm pheromones, plus a wide variety of substances which facilitate chemical communication among various species in the biocenosis (called allelochemical compounds in the foreign literature).

These include the allomones (scents or toxins which are aversive to foes) and kairomones (chemical agents used by entomophags to locate insect hosts and victims. In a broad sense, they are substances necessary not only to the organism which secretes them, but also to the organism which senses them and reacts to them.

An acquaintance with research trends on biological active substances in the US gives an impression that this line of research is considered to be the main prospect for discovering new plant protection agents.

The British-American publishing company, Plenum Publishing, has published the Journal of Chemical Ecology quarterly since 1975. This journal reports on modern achievements in the study of the chemical structure of natural compounds and the need for close contact and coordination between chemists and biologists as being a major prerequisite for advancing the knowledge of interaction among organisms in nature. In 1976, the journal published 42 articles, most of which dealt with insect and mammalian pheromones. Of the hormone compounds, the most attention was given to juvenile hormone analogs (juvenoids).

The natural juvenile hormone of insects was identified in 1965-1973 by American scientists. These studies proved the existence of at least three forms of juvenile hormone within an insect class: JuH-1, JuH-2 and JuH-3. Their chemical nature is very similar to the sesquiterpenes and they are derivatives of farnesyllic acid. On-going efforts in the US and other countries to discover, identify and study

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the biological properties of various forms of JuH and their analogs may provide a base for reverse synthesis of biologically active compounds which have a selective effect on specific insect groups.

Czech investigators have been carrying on a continual quest for new ways and means of employing synthetic hormonal analogs. Research is continuing in the study of the systemic nature of action of juvenogens. A distinctive feature of these compounds is their ability to change into substances having juvenile-hormonal activity in response to some biological or internal factor, but remain dormant prior to that point.

In addition, work has recently begun on the study of precocenes (antijvenile hormone).

Juvenoids have already been widely tested in pest control. In 1976, treatment of the mulberry tree against the first generation of the fall webworm in the Novoanensk region of the Moldavian SSR completely prevented a scourge by this species.

Considerable interest is afforded by another group of hormone-like compounds: chitinization inhibitors, which have been undergoing tests here and abroad for three years. These compounds are for the most part enteric in action and may be successfully employed against a wide range of leaf-eating pests. Preliminary tests have demonstrated the high efficacy of the most active of these compounds: Dimilin® [difluorn] (active principle is difluorobenzoyl urea) against such destructive pests as the turnip moth, cutworm, beet webworm, fall webworm and others. Dimilin® and allied compounds are not only non-toxic to humans and warm-blooded animals (LD₅₀ ranges from 10,000 to 19,000 mg/kg), but they are also of low toxicity to most entomophags. The exceptionally high biological activity of Dimilin® accounts for the small quantity of Dimilin® required for treatment. For example, a mere 0.03 kg per hectare is virtually 100 percent effective against the fall webworm.

The bibliography on insect pheromones is extensive. In 1976, M. Jacobson's thorough compendium "Sex pheromones of insects" was published in Russian and the review "Pheromones and hormonal compounds in the US" (Moscow, 1976) by Ye. M. Shumakov, V. N. Burov and A. I. Smetnik added new data to Jacobson's book.

In recent studies, lists have been published of all identified sex pheromones according to the latest data in 1976. The American chemical manufacturer Zoecon produced a rather wide variety of pheromones in 1977 for various insect pests. Pheromone-baited insect traps have appeared on the market for 25 species of Lepidoptera and sexual attractants for four species of Drosophila. Among the pheromones for Lepidoptera, interest has been stimulated by traps for the codling moth, oriental fruit moth, gypsy moth, grape-berry moth and European corn borer, which are dangerous pests in the USSR as well.

Many sexual pheromones of destructive moths have been synthesized and studied in the USSR; the results of this research have been discussed in several of the reports appearing in this collection.

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Pheromones of the true bugs have not been thoroughly investigated; in fact, to date no single compound has been identified which could be considered a pheromone of any species of Hemiptera. Meanwhile, in true bugs one would expect a wide diversity of pheromones, including sexual, trail and territorial marks. The significance of this problem is defined in particular by the fact that among Hemiptera, there are very many serious pests, such as the destructive shield bug (*Eurygaster*). Studies by entomologists of the All-Union Institute for Protection of Plants (VIZR) and the Institute of Entomology of the Czechoslovak Academy of Sciences, in particular, have demonstrated that compounds of the vanillin type play some role in sexual communication in the shield bugs and are attractants to females.

In 1975, collaboration was begun between the sterilization laboratory of VIZR and the Laboratory of Natural Compound Chemistry of Leningrad University, with the aim of identifying the pheromones of the shield bug. In view of the low volatility of vanillin, it would be anticipated that the sexual pheromones of the shield bug also serve as markers and their individual components can be identified.

In addition to sexual pheromones of destructive insects, research on bee pheromones is worthy of note; among these, the decenoic acids have been studied in the greatest detail. Some of them have been synthesized by the Shchelkov branch of the All-Union Scientific-Research Institute of Chemicals Used for Plant Protection (VNIKhSZR) and have been tested by several scientific institutions.

In the bee family, (E)-9-Oxo-2-decenoic acid (KDA), or Queen Substances, was identified as an inhibitor of reproductive activity in worker bees. The domestically produced KDA synthesized by coworkers at the Shchelkov branch of VNIKhSZR (Kyskin, Pyatnova, et al., 1971) was investigated at the insect sterilization and attractant laboratory of VIZR on bees and destructive insects.

Synthetic KDA appears to function biologically by retarding ovarian development in the worker bee in queenless colonies and affects their laying of queen bee eggs. A substrate treated with 1 percent KDA in a form resembling a queen bee caused bees in a queenless colony to form a retinue around it similar to the retinue formed around a live queen bee.

Laying workers have been successfully controlled with KDA. The return of worker bees with active ovaries to their normally inactive state with KDA is of tremendous practical significance in apiculture to control laying worker development; and offers the prospect that KDA can be used to suppress reproduction of destructive insects. Furthermore, KDA applied to the body of a queen bee is successful even when it is transplanted into a laying bee colony. Colonies in which laying bees have developed will generally not accept the queen bee and will inevitably kill her.

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In 1977, the role of KDA in improving flight pollination activity of queenless bee layers was demonstrated in hothouses in the Leningrad oblast; this offers promise for using KDA in hothouses to intensify the pollinating activity of bees. Experiments are also in progress on the use of KDA as a chemosterilant for destructive insects.

More than 100 compounds have been tested at the laboratory of insect sterilization and attractants of VIZR with the goal of finding effective chemosterilants for insects of various orders. Compounds with high sterilizing activity have been found among the derivatives of ethylenimine, embikhin [methylchloroethamine HCl], ethylenamines of phosphoric and thiophosphoric acids, derivatives of phosphonitrylchloride, allylamines of phosphoric acids, hormonal compounds, and so forth. As a result, sterilizing doses have been established and methods have been developed for chemical sterilization of 13 species of destructive insects. As illustrated by the codling moth and the true bug (the shield bug), the mechanism of action of ethylenimine derivatives on oogenesis has been studied; one of its manifestations is suppression of nucleic acid synthesis. The effect of "inherited sterility" which occurs in response to substerilizing doses of ethylenimine derivatives has been studied in the codling moth, turnip moth and graphosoma bug.

Research into kairomones carried out by American scientists, mainly at Pennsylvania University, made it possible to isolate and synthesize two kairomonic communication systems:

for the corn earworm (*Heliothis zea*) and its parasite *Trichogramma evanescens* and the predator *Chrysopa carnea*;

for the potato moth (*Phthorimea operculella*) and its parasite *Orgilus lepidus* Muesb. (of the Braconidae).

As has been discovered, in the first case, the squamulae of the corn earworm contain kairomones which attract *Trichogramma* and *Chrysopa*. A hexane extract of earworm squamulae was used to identify the kairomones. Kairomones from the earworm squamulae were found to be C₂₁-C₂₅ hydrocarbons. The especially saturated hydrocarbon C₂₃ was found to be extremely stimulating to the quest reaction of *Trichogramma*.

The kairomone system in the potato moth is a mixture of normal aliphatic acids. One of them, heptanoic acid, greatly intensifies the quest reaction of the parasite.

Chrysopa is highly attracted to the honeydew secreted by aphids and other suctorial insects, and the substances it contains stimulate egg laying of *Chrysopa*. Some amino acids were narrowly defined as attractants in this context.

In 1975, research by entomologists at Pennsylvania University first demonstrated that substances which are kairomonic are widely represented among the forage plants of these pests: in maize and potato tubers; in other words, insect kairomones are of vegetable origin, as has been proven for insect hormones.

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These groups of compounds far from exhaust all the biologically active substances of value in plant protection. The expansion of research into the diverse groups is a major subject for further investigation.

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PROSPECTS FOR INDUSTRIAL PRODUCTION OF INSECT PHEROMONES

Moscow BIOLOGICHESKI AKTIVNYYE VESHCHESTVA V ZASHCHITE RASTENIY
in Russian 1979 pp 9-13

[Article by Yu. B. Pyatnova, candidate of chemical sciences]

[Text] The existence of chemical communication in the insect world has by now been thoroughly demonstrated. Knowledge of the chemical structure of natural regulators allows man to control insect behavior. Insect sexual pheromones have been widely used for this purpose.

In the US, attractants are produced and widely used for the codling moth (Codlemone®), oriental fruit moth (Orfomone®), plum moth (Funemone®), leaf-roller moth, cotton leaf miner, and gypsy moth.

Practical interest in pheromones makes it necessary to develop preparatory methods of synthesis. We have developed means of pheromone synthesis for the plum, oriental fruit, codling and gypsy moths.

When these substances are being synthesized, we consider the need to obtain substances which are maximally pure, free of impurities, including geometric isomers; we therefore select methods having high stereospecificity.

The plum moth attractant is Z-8-dodecenyl acetate. The acetate containing 97 to 98.5 percent of the Z isomer and 1.5 to 3 percent of the E isomer has the highest biological activity. After investigating several methods of synthesizing Z-8-dodecenyl acetate for pilot production, we recommended a method based on alkylation of 1-sodium pentene of chloroheptanoic acid. The resulting 8-dodecenoic acid is recovered with lithium aluminum hydride in the appropriate alcohol, hydrated into Z-8-dodecenol and acetylated. The experimental installation was planned and assembled according to this arrangement. In the course of three years we have produced rather large test batches which have been used to study preparatory forms and for developing application methods.

The attractant of the oriental fruit moth is a mixture which includes one part Z-8-dodecenyl acetate containing 7-8 percent of the E isomer and 92 to 93 percent of the Z isomer; ten parts of dodecyl alcohol. Therefore, by solving the problem of producing Z-8-dodecenyl acetate, we also obtain the attractant

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of the oriental fruit moth. The required proportion of Z:E isomers is achieved by mixing Z-8-dodecenyl acetate and E-8-dodecenyl acetate obtained by recovery of the alkene precursor by sodium in liquid ammonia.

Z-8-dodecenyl acetate is also an inhibitor of perception by the codling moth of its own sexual pheromone. At VIZR, its possible use to control sexual mating in the codling moth is being investigated.

The natural attractant of male codling moths is E, E-8, 10-dodecadienol. The presence of other geometric isomers in the synthetic pheromone is undesirable, since this reduces its biological activity and sometimes totally inhibits it.

Our goal was to synthesize E, E-8, 10-dodecadienol with high biological activity. Several methods of synthesis of E, E-8, 10-dodecadienol have been developed. The most suitable for preparatory purposes is the method which uses the Whiting reaction to create a system of conjugated double bonds.

Phosphonic acid obtained from 8-bromooctanoic acid and triphenylphosphine, with treatment by sodium methylsulphonylmethylide in DMSO (dimethylsulfoxide) yields the phosphoylide, whose interaction with croton aldehyde produces the 8,10-dodecadienic acid.

Dodecadienic acid obtained in the Whiting reaction under these conditions is a mixture of two isomers: primarily Z-8, E-10 isomer and partly the E, E-8, 10-isomer. This acid is recovered by lithium aluminum hydride in alcohol. In order to increase the content of the E,E-isomer, the alcohol is isomerized in UV light in the presence of catalytic quantities of iodine. Pure E, E-8, 10-dodecadienol is obtained by low-temperature crystallization from pentane.

The described method of synthesis, however, contains technological difficulties which prevent it from being put into production. We therefore continued our quest for practical methods of synthesis of E, E-8, 10-dodecadienol.

In field tests conducted by T. P. Bogdanova at VIZR, the dodecadienol which we synthesized actively attracted male codling moths into the traps and was just as effective as Codlemone®, the compound produced by Zoecon. Application forms are currently being developed which are suitable for supervision and regulation of the codling moth population.

We have also synthesized the attractant of the gypsy moth, Z-7,8-epoxy-2-methyloctadecane (Disparlur®) by two methods. Starting with 2-methylhexane, by hydrobromation against the Markovnikov rule, we obtain 2-methyl-hexyl-bromide. From decylbromide with sodium acetylenide we obtain dodecene-1, whose lithium product is alkylated with 2-methylhexylbromide. The alkene is stereodirectionally hydrated to the cis-alkene and is epoxidated. High purity (99.7 percent) Disparlur® is obtained. It is extremely high in biological activity: at a dose of 0.05 microgram it is active for the entire flight period of the gypsy moth, i.e. for 45-50 days.

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Disparlur® has also been synthesized according to the Whiting reaction. From isoamylmagnesium bromide and allylbromide, the isooctene is obtained which upon hydrobromation yields the isooctylbromide. The phosphonic salt obtained from the isooctylbromide and triphenylphosphine with sodium methylsulphinyl-methylide leads to the corresponding ilide which, with undecanol, yields 2-methyl-Z-7-8-octadecene. Disparlur® is obtained after epoxidation.

After comparing the biological activity if Disparlur® obtained by these methods and the economic indicators we shall select a method for industrial production of the attractant.

For several years, N. G. Shaposhnikova at VIZR has been studying the biological effect of (E)-9-Oxo-2-decenoic acid, one of the components of Queen Substance of *Apis mellifera*. She demonstrated the possibility of using this acid in apiculture to prevent swarming, for prevention and correction of the laying worker activity in bee colonies and to facilitate transplantation of queens. (E)-9-Oxo-2-decenoic acid inhibits reproductive activity in other insects: in the fly *Drosophila phalerata*, in the shield bug, and in the rapeseed sawfly. This opens up the possibility for using oxydecenoic acid to control destructive species as a natural chemosterilant.

In view of the applied value of (E)-9-Oxo-2-decenoic acid, we developed two methods to synthesize this compound based on 7-chloroheptanoic acid. Bromation and dehydrobromation changes the initial acid to (E)-7-chloro-2-heptenoic acid and this is converted into (E)-7-iodo-2-heptenoic acid. Condensation of the latter with sodium acetic ester accompanied by alkaline hydrolysis yields (E)-9-Oxo-2-decenoic acid. Another version includes reaction of 7-chloroheptanoic acid with methyl lithium, conversion of the resultant 1-chloro-octane-7-one to the oxyketone; oxidation of the latter to 7-ketooctanol and its condensation with malonic acid.

Both versions of synthesis are simple and may be reproduced on an industrial scale. After specific recommendations for practical application, a pilot plant can be established for production of (E)-9-oxo-2-decenoic acid.

Therefore, we have developed preparatory methods of synthesis of several attractants of the most prevalent and dangerous pests of agricultural crops. This will make it soon possible to introduce safe, effective methods of supervision and control of the development of these species in plant protection.

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PROSPECTS FOR USING POLYMER MATERIALS TO PROLONG THE EFFECT
OF ATTRACTANTS

Moscow BIOLOGICHESKI AKTIVNYYE VESHCHESTVA V ZASHCHITE RASTENIY in Russian
1979 pp 13-18

[Article by A. I. Terekhova and L. I. Verzunova, candidates of chemical sciences]

[Text] The creation of compounds having reliable control of diffusion of the
active principle is one of the chief problems in the use of synthetic pheromones.

Among the various methods for tackling this problem, methods using polymers
have become most prevalent: prolongation of the action of the attractants is
achieved by diffusion from polymer/attractant composites or through polymer
films. In the first instance, the polymer is a matrix containing an attractant
whose diffusion depends on the physico-chemical properties of the polymer and
attractant. Various thermoreactive polymers, synthetic or natural rubbers can
be used as the matrix material. Polyurethanes, PVC, polyvinylpyrrolidones
(povidones) and polyethylene glycol have been used; fillers (chalk, clay) are often
used to preform the compounds. The attractant can be added to the polymer
by mixing it with the initial components. If vulcanized rubber is used as the
matrix, favorable conditions for diffusion of the attractant into the polymer are
created when there is swelling in the attractant or in its solution. The swelling
method can be used to prepare very large batches in a short time. But this
method is deficient in that during the swelling process certain components may
be removed from the polymer and the specimens lose their strength and
elasticity; nonproductive losses of attractant are also possible. Thus for
industrial use, preference should be given to the method of premixing of
attractant and components of the rubber mixture.

Compounds have lately been prepared in our country for primary biological tests
of attractants of the oriental fruit and plum moths consisting of rubber based
on natural rubber employing the method of swelling in their solutions.

The solvent should have the following properties: rather high degree of swelling,
absence of destructive effect on the polymer, high volatility. The latter
property is necessary so the solvent leaves the specimen in a short enough time
and does not induce an untoward side effect while the compound is working.
Chloroform, hexane and p-xylene have been tested as solvents. The parameters

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of solubility which characterize the intermolecular interaction of polymer and these solvents are equal to, respectively, Δ hexane = 7.3 + 7.4; Δ chloroform 9.3; Δ p-xylene 8.8; Δ natural rubber 8.1. Degrees of impregnation of rubber based on natural rubber in these solvents were determined: α chloroform = 4.25; α hexane = 0.89; α p-xylene = 2.16 (t = 22°C). Chloroform has a strong destructive effect on rubber and thus the final products used were hexane and p-xylene. In view of the difference in physico-chemical properties of attractants of the oriental fruit and plum moths, it was necessary to determine the variation in degree of impregnation (α) of the polymer in solvents as a function of their concentration. The results proved that α linearly varies from 2.75 (C = 5 percent) to 1.77 (C = 100 percent) for attractants of the plum moth and for the attractant of the oriental fruit moth from 2.6 (C = 5 percent) to 0.4 (C = 90 percent). Because diffusion of cis-8-dodecenyl acetate and dodecyl alcohol into the impregnating polymer may be different, solutions were analyzed before and after impregnation by the gas chromatographic method. Tests showed that the proportion of components had not changed.

The maximum degree of impregnation was attained after several hours, and it was determined by the weight of the specimens before (m_0) and after impregnation (m_{\max}):

$$\frac{m_{\max} - m_0}{m_0} .$$

An important part of the development of pheromone compounds is the analysis of the working characteristics of the compound: consumption of attractants, duration of effect, resistance to various environmental factors during testing.

The rate of release of attractants from the compound was determined by weight loss of the specimen subject to conditions close to natural ones (temperature and air velocity).

The kinetics of specimen weight change produced by impregnation in solutions having a different concentration of plum moth attractant (solvent p-xylene) shows a sudden drop in weight in the first few hours due to release of the solvent; with a reduction in the percentage content of the solvent, the curve becomes flatter. As these data suggest, the solvent is released almost completely in the first three to four hours; then the slope of the rectilinear segment of the curve may be considered a constant which quantitatively describes the consumption of attractant. Curves of the kinetics of release of oriental fruit moth attractant from a rubber-based compound are the same. In view of the dual componential nature of the oriental fruit moth attractant, it is also necessary to refine the composition of the attractant released from the compound. According to modern concepts, the molecules diffused in the polymer experience double resistance: "lateral" and "frontal." Lateral resistance is proportional to the number of atoms in the diffusing molecule, while frontal resistance is proportional to the cross section. Dodecyl alcohol and cis-8-dodecenyl acetate have negligibly different characteristics in this case and no

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substantial change in the composition of the gaseous phase was anticipated. Gas chromatography corroborated this assumption.

Data on the kinetics of release of attractant from the composite make it possible to determine its overall reserve in terms of the difference in weight of the specimen in the linear segment of the curve and a control specimen impregnated in pure solvent (Δm). A comparison of the relationships of doses (Δm) of pheromone in specimens as a function of solution concentration in which they were produced shows that for the plum moth attractant, the dose increases linearly, while for the oriental fruit moth this relationship has a limit. This would suggest that to prepare the plum moth attractant composite by the impregnation method, the entire range of concentrations is suitable; and the criteria for selecting conditions should be the requirements imposed on attractant consumption, desired period of effect, etc. For the oriental fruit moth attractant, an increase in solution concentration from ten to ninety percent yields no substantial increase in its dose in specimens and therefore, an increase in concentration of the active principle in technological solutions of more than 10 percent is unprofitable.

Analysis of the rate of release of this attractant and the periods of effect of compounds calculated by the formula $t = (\Delta m)/v$ (Δm = dose in milligrams, v = consumption of attractant in milligrams/day) showed that an increase in the period of effect is observed when switching from 5 percent to 10 percent solutions. With a further increase in concentrations of the solutions, the rate of diffusion varies in direct proportion to the doses of the active principle in the composite and the estimated periods of effect remain constant (about 50 days).

Table. Relationship of the Rate of Release as a Function of Dose of Oriental Fruit Moth Attractant in a Polymer/Attractant Composite

Content of attractant in hexane solution, percents	Content of attractant in specimen, milligrams	Rate of re- lease of at- tractant, mg per day	Period of effect
5	12.5	0.7	16.0
10	40.0	0.8	50.0
20	74.5	1.4	53.0
50	100.0	2.1	50.0
70	100.0	2.1	50.0
100	90.0	1.8	50.8

Polymer/attractant preparative forms of Disparlur® prepared by the impregnation method also demonstrate high biological activity. The concentrations of attractant in this case were extremely small: 0.5 to 5 micrograms per specimen. Consumption of Disparlur® from preparative forms was not measured due to the inadequate sensitivity of the weight method.

In addition to composites in which the polymer is a matrix, composites are also used in which the dosage of attractant into the environment is carried out by diffusion through a polymer diaphragm. Polymer ampules and capsules which

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were tested for attractants of the plum, oriental fruit, codling and gypsy moths are this type of composite.

Ampules were made of polyethylene and polypropylene tubes with a wall thickness of 0.5 millimeters and capacity of 0.04 milliliter. The weight method was used to study the kinetics of release of plum moth attractant from polypropylene ampules with a capacity of 40 microliters and wall thickness of 0.5 millimeter. For this purpose, specimens of the composite were kept in a well-ventilated room and were weighed at specific intervals to within 10^{-4} gram; temperature was changed in a rather wide range, from 18 to 35°C. In the course of six months, consumption of attractants was constant and equalled 0.2 to 0.4 milligrams per day.

Results of investigation of the kinetics of release of plum moth attractant show that in the initial period (several days), much less of the active principle was released than in the remaining time. We attribute this phenomenon to the distinctive features of the mechanism of permeability of the polypropylene film. As we know, sorption of the substance by the membrane and its impregnation is the first stage in the process of penetration through the polymer membrane. The microencapsulation form was also tested for these pheromones. Encapsulation of the two percent solution of attractant was carried out by the method of complex coacervation using gelatin and polyacrylic acid. The capsules with a degree of dispersion of 1.0 to 1.5 millimeters were applied on paper with the aid of a special composition containing methyl cellulose and latex.

The gelatin envelopes of the capsule have considerably different permeability than polypropylene ampule envelopes. This is proven by the fact that the solvents (p-xylene, benzene, hexane, etc.) diffuse from polymer ampules at a rate of 40 milligrams per day or more, whereas for the microencapsulated form this rate is 0.2 to 0.4 microgram per day. This is the result of a difference in the structure of polymers and the interaction of the polymer and liquid medium.

The microencapsulated form of attractants allows us to widely alter the rate of diffusion by varying the concentration of the active principle in the encapsulation phase and consequently, the concentration of attractants in the air. This is especially useful for the Disparlur® attractant of the gypsy moth and codling moth attractant, because the attraction effect is observed at extremely low concentrations. To test capsules containing a 0.2 percent solution of attractants in p-xylene, they were applied on paper in quantities corresponding to specific doses of the active principle.

These results would suggest the promise of preparative forms of pheromones based on polymer materials.

It should be noted that all the possible kinds of preparative forms of sexual pheromones of insects have not been covered in this report. Future studies on synthesis and tests of the spectrum of effect of pheromones will probably widen this list in terms of their physio-chemical and biological properties.

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INVESTIGATION OF INSECT SEX PHEROMONES AT THE ALL-UNION SCIENTIFIC-RESEARCH INSTITUTE OF BIOLOGICAL METHODS FOR PROTECTION OF PLANTS (VNIIBMZR)

Moscow BIOLOGICHESKI AKTIVNYYE VESHCHESTVA V ZASHCHITE RASTENIY
in Russian 1979 pp 18-23

[Article by B. G. Kovalev, candidate of chemical sciences, VNIIBMZR]

[Text] The need for industrial production of insect sex pheromones is mainly dictated by the existence of completed technological developments for their application, i.e., the readiness of producers to use sex pheromones in practice. With the exception of quarantine pests, whose technology of employing pheromones is comparatively simple and requires no long-term research, a great deal of time is required to develop methods for employing sexual attractants for the remainder of pests. In the near future, the most likely use of sexual attractants will be in plant protection as a means of supervision and prediction of the pest population. Because of the simplicity of handling and low cost of sexual pheromone-baited traps, the existing structure of the warning service can be altered. Plant protection agronomists at any sovkhoz or kolkhoz will be able to easily and reliably determine not only the onset of flight of a pest according to the traps, but also determine the need for chemical treatments. This last item is extremely important, because it not only permits improvement of the economics of protective measures, but also stimulates the local entomological fauna and reduces environmental pollution.

Thus research at VNIIBMZR in sexual pheromones of insects has been carried out along two fundamental lines: 1) identification of sexual pheromones of insect of economic importance and 2) development of utilization technology.

When integrated systems of crop plantation protection are employed, in addition to the chief pests such as the codling moth, San Jose scale and others, a large group of leaf rollers is important since they destroy from 12 to 20 percent of the harvest, or as high as 50 to 70 percent in years of mass multiplication. For this reason, we began systematic research to find effective lures for the pests of this group. Studies carried out in 1977 established the chemical composition of the sex pheromone of the currant leaf-roller *Pandemis ribeana*. It was a mixture of cis-trans-isomeric acetates of 11-tetradecenol. Field tests demonstrated the high attractiveness of the sex lure.

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The sex pheromones of the omnivorous (*Archips podana*), reticulated (*Adoxophyes reticulana*) and rose (*Archips rosanus*) leaf-rollers are known. Their chemical composition is shown in Table 1.

Using arrangements earlier developed by us, synthesis of the components of sex pheromones of these species of leaf-rollers has been effected and they have been field tested; the results are shown in Table 2.

Table 1. Chemical Composition of Sex Pheromones of Three leaf-Roller Species

Leaf-roller species	Composition of pheromone (proportion of components)
omnivorous	$\begin{array}{c} \text{cis} \qquad \qquad \qquad \text{trans} \\ \text{C}_2\text{H}_5\text{CH}=\text{CH}(\text{CH}_2)_{10}\text{OAc} + \text{C}_7\text{H}_5\text{CH}=\text{CH}(\text{CH}_2)_{10}\text{OAc} \\ (1:1) \end{array}$
rose	$\begin{array}{c} \text{cis} \qquad \qquad \qquad \text{cis} \\ \text{C}_7\text{H}_5\text{CH}=\text{CH}(\text{CH}_2)_{10}\text{OAc} + \text{C}_2\text{H}_5\text{CH}=\text{CH}(\text{CH}_2)_{10}\text{OH} \\ (9:1) \end{array}$
reticulated	$\begin{array}{c} \text{cis} \qquad \qquad \qquad \text{cis} \\ \text{C}_4\text{H}_9\text{CH}=\text{CH}(\text{CH}_2)_8\text{OAc} + \text{C}_2\text{H}_5\text{CH}=\text{CH}(\text{CH}_2)_{10}\text{OAc} \\ (9:1) \end{array}$

Table 2. Attractiveness of Synthetic Lures for Males of *A. podana*, *A. rosanus*, *A. reticulana* and *P. ribeana*

Leaf-roller species	Dose (mcg)	Males captured (avg.) per trap in 14 days
omnivorous	2000	24.5
	Control	0.0
rose	2000	68.0
	Control	
reticulated	2000	28.2
	Control	0.0
currant	2000	22.5
	Control	0.0

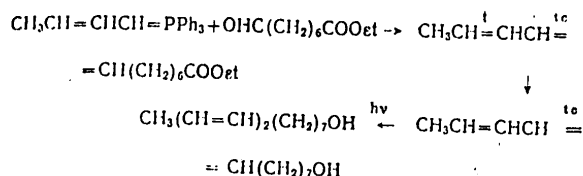
Along the same lines of integrated orchard protection, we began a study of the sex pheromones of two species of the genus *Orgyia*: *Orgyia gonostigma* (tussock moth) and *orgyia antiqua* (vaperer moth). These two species represent a considerable threat to intensive type orchards and a battle must be fought against them some years in Moldavia. We know that the sex pheromone of the American species *Orgyia pseudotsugata* is the unsaturated keton cis-6-geneycosen-11-one. Field tests of this substance demonstrated its high attractiveness for males of *O. antiqua*. Males of the species *O. gonostigma* were not attracted by this substance. The results of field tests are shown in Table 3.

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Table 3. Catch of Males of *O. Antiqua* in a Trap with Cis-6-Geneycose-11-one (observations of four traps over 6 days)

dose (mcg)	Males captured (average) per trap in six days
1000	13.2
100	6.0
10	4.5
Control	0.48

Using the arrangement:



the attractant of the codling moth, Codlemone®, was synthesized in 1976. The activity of the substance is as good as the lures manufactured by Zoecon. Testing of specific doses (Table 4) under field conditions showed that there is no significant difference between a dose of 2000 mcg and the compound produced by Zoecon.

Table 4. Attractiveness of Various Doses of Codlemone® for Male Codling Moths (20 days)

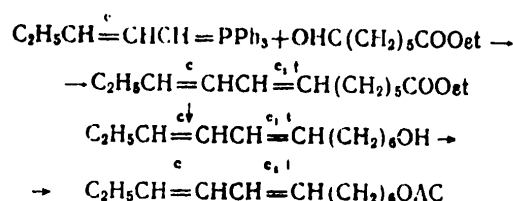
Test version	Number of males captured by repetitions				Sum	Average
	1	2	3	4		
Codlemone dose, mcg:						
100	75	88	64	74	301	75.25
1000	197	72	90	126	385	96.25
2000	142	138	138	131	549	137.25
Compound of Zoecon	127	130	123	136	516	129.0
HCP ₀₅ = 24.0						

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The existence of an active compound made it possible in 1976 to begin development of an application technology. Since 1977, in Moldavia traps containing Codlemone have been used in a 5,000 hectare area to signal the onset of flight of the codling moth, that is, to signal the start of the struggle against it. In a 500 hectare area, a pilot industrial test is being done on traps with Codlemone to make the use of traditional toxic chemicals more efficient. During the 1977 season, VNIIBMZR regularly supplied capsules with Codlemone to the Armenian NIIZR, Ukrainian Scientific-Research Institute of Horticulture, and the Scientific-Research Zonal Institute of Horticulture of the Nonchernozem belt of the RSFSR.

VNIIBMZR has developed a method to obtain a mixture of isomeric acetates of 7,9-dodecadien-1-ol, wherein 7-trans-9-cis-isomer is a sex attractant to the leaf roller moth *Lobesia botrana*.

Synthesis was performed as follows:



Field tests of various specimens of sex pheromone made it possible to select the most promising one which was just as active as Zoecon's (Table 5).

Table 5. Attractiveness for Males of *L. botrana* of a mixture of cis,trans-isomeric acetates of 7,9-dodecadien-1-ol

Substance	dose, mcg	Males captured (average) per trap
Ferocone (USA)	—	134.6
Ferocone (VNIIBMZR)	2000	116.3

In 1977, the compound was studied in all zones of Moldavia to signal the start of the struggle against this pest. A pilot test using this method has been running on farms in Moldavia since 1978.

In 1977, the compound was widely used at ArmNIIZR where about 800 capsules with this pheromone were delivered.

As a result of systematic research to find sex attractants of cutworms, the most dangerous agricultural crop pests, the attractant of the cabbage moth *M.*

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brassicae was identified as cis-11-hexadecen-1-ol acetate. The substance was tested under field conditions and was found to be an extremely active attractant (Table 6).

Table 6. Attractiveness for Males of *M. brassicae* of Cis-11-hexadecen-1-ol acetate (observations of five traps for 24 days)

Test version (dose in mcg)	Males captured (average) per trap
2000	31.0
one female	10.0
control	0.0

We tested the cis, trans-isomeric acetates of 11-tetradecen-1-ol and their mixtures for attractiveness to males of the European corn borer *Ostrinia nubilalis*. Mixtures with low content of the trans-isomer were active.

In 1977, in an area of 400 hectares, a pilot industrial test was begun of the method of gypsy moth population prediction with the aid of Disparlur®, the sexual attractant of this species.

According to the decisions made by the convention on prospects of industrial production of attractants for fruit moths (1976), VNIIBMZR has conducted research and found an original trap design for catching fruit moths and leaf rollers which is just as efficient as the traps made by Zoecon. Effective trap designs have been tested and selected for capturing male earworms and the gypsy moth.

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SOME DATA ON THE VOLATILITY AND STABILITY OF ATTRACTANTS

Moscow BIOLOGICHESKI AKTIVNYYE VESHCHESTVA V ZASHCHITE RASTENIY
in Russian 1979 pp 47-49

[Article by F. P. Vayntraub, candidate of agricultural sciences; L. P. Dron', Ye. V. Gitsiu, L. S. Keyser and L. L. Chernichuk, All-Union Scientific-Research Institute of Biological Methods of Plant Protection]

[Text] The success of pheromone communication depends on the properties of the pheromones themselves as well as on many environmental factors. The volatility of compounds, the effect on this process of temperature, humidity, wind, the nature of the substrate, initial concentration, etc. are very important.

The stability of attracts in the environment also governs their effective use.

In model tests at fixed temperature (25°C) and wind velocity of 1.5 meters per second, the effect of the substrate and concentration on the volatility of gypsy moth attractant was studied. Some 250, 500 and 1000 micrograms of Disparlur® in one milliliter of hexane were applied to strips of filter paper 5 x 13.5 centimeters in size; 1000 and 2500 micrograms were applied to strips of foil of the same dimensions. The amount of unevaporated compound was determined by gas-liquid chromatography (GLC).

On various substrates, the loss of Disparlur® at a given concentration occurs at different rates. It is a geometric process.

Regardless of the initial concentration, the loss of compound is more rapid in the first 6 hours and slows down after 24 hours (regardless of initial concentration).

In field tests of these concentrations in traps, the rate of loss correlated well with laboratory data.

The rate of evaporation of the oriental fruit moth attractant (mixture of cis-8-dodecenyl acetate with 7.5 percent trans-8-dodecenyl acetate and addition of dodecylic alcohol (a synergist) in a proportion of 1:10, pheromone synergist) was studied in laboratory and field tests. GLC methods determine the components in a PVC composite.

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In the laboratory test (temperature 20-23°C, wind velocity 2.3 meters per second), relationships which define the rate of evaporation of the attractant in time were calculated:

$$\text{for cis-8-dodecenyl acetate } \log y = 1.03 - 0.097 x,$$

$$\text{for dodecyl alcohol } \log y = 2.23 - 0.17x,$$

where y is the rate of evaporation, mcg/hour;
x is time in days.

The field test completed in July 1976 showed that over the course of a month about 80 percent of the initial quantity of cis-8-dodecenyl acetate evaporates.

For the attractant of the codling moth (trans, trans-8, 10-dodecadien-1-ol), GLC methods were developed for analysis in rubber-based composites. Evaporation of the attractant was studied in field tests in May/June, 1977.

The relationships to which the attractant evaporation process is subject when applied in the trap at various concentrations come to:

$$\text{at 1000 mcg, } y = 176 e^{-0.305 x^{0.577}} \cdot x^{-423},$$

$$\text{at 1500 mcg, } y = 309 e^{-531 x^{0.388}} \cdot x^{-612},$$

$$\text{at 2000 mcg, } y = 403 e^{-0.476 x^{0.423}} \cdot x^{-0.577},$$

where y is the rate of evaporation, mcg/day and x is time, in days.

This process, like for Disparlur®, is characterized by high initial rate (150 to 200 mcg/day) in the first five days. Then, regardless of the amount of substance applied, the rates equalize (20-30 mcg/day).

It may be assumed that such model tests will permit prediction of periods of replacement of attractant sources in traps.

Among the factors affecting the stability of compounds in the environment, we have specified light (UV and sunlight) and pH of the medium.

Irradiation of Disparlur® in quartz test tubes with a UV source (80 percent at wavelength of 365 nm) for 20, 60 and 80 hours led to a loss of up to 80 percent of the compound (quantum output $\Phi = 0.5 \times 10^{-4}$). Research is now being carried out to study the effect of sunlight on the loss and degradation of Disparlur®.

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ADVANCED MEDICAL TECHNOLOGY

IMMOBILIZED BIOPREPARATIONS IN MEDICINE

Moscow IMMOBILIZOBANNYYE BIOPREPARATY V MEDITSINE
in Russian 1980 signed to press 16 Nov 79 pp 2-4, 125-126

[Annotation, introduction and table of contents from book "Immobilized Biopreparations in Medicine", by Konstantin Alekseyevich Makarov and Sergey Alekseyevich Kibardin, Izdatel'stvo "Meditsina", 6,000 copies, 128 pages]

[Text] Different aspects of the use of enzymes, hormones, antibiotics and other drug agents, which are fixed (immobilized) in organic and inorganic copolymers (carriers) are examined in this monograph. The characteristics of such carriers are described and the methods to produce the immobilized biopreparations, their properties and the nature of their application in medicine are outlined. The authors discuss the relative advantages of immobilized preparations in comparison with analogous soluble preparations. Data are presented on the use of immobilized preparations for therapeutic purposes: to process blood, correct enzyme insufficiency in an organism and as anti-cancer preparations. Promising aspects of and results from the use of immobilized biopreparations in surgical clinics are examined. The possibility of using them in chemico-pharmaceutical manufacturing is discussed.

The book is written for workers involved in clinical medicine, instructors, biochemists and workers in chemical-pharmaceutical manufacturing. 2 figures; 4 tables; bibliography: 169 references.

Introduction

The term "immobilized preparations" is used to designate all types of insoluble derived enzymes, hormones, antibiotics and those compounds which are modified in solution by copolymers. According to the recommendations of the International Commission on Enzyme Technology for Enzyme Modification by Physical-Chemical and Chemical Methods, enzymes can be divided in two large groups: embedded and coupled. Enzymes included in the structure

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of organic and inorganic copolymers belong to the embedded group. Enzymes which are adsorbed by various physical-chemical methods in hard carriers (matrices) belong to the coupled group as well as those which are coupled with hard carriers in chemical compounds. All such compounds are called immobilized enzymes. The more general term--immobilized biopreparations--is used to designate immobilization of various biologically active compounds (enzymes, antibiotics, hormones and other drug compounds).

Immobilized biopreparations can be used for diagnosis and treatment of various diseases, as well as for production of more modern prostheses and apparatus which are used to replace some of the most important human organs. Methods for immobilization have provided new ways to construct apparatus for an artificial kidney and liver. Thus, using immobilized urease, successful tests were conducted on the portable apparatus for an artificial kidney.

In the opinion of a number of specialists, the era of enzymes has replaced the era of antibiotics and hormonal preparations. However, widespread use of enzymatic preparations is limited by their relative instability during storage, rapid inactivation in the internal environment of the organism, the strong immunologic reaction to them, their high cost and the impossibility of regeneration. These inadequacies could be eliminated to a significant degree by immobilization of enzymes; that is coupling them with inorganic and organic polymers.

Immobilized enzymes have been used successfully to eliminate various harmful metabolites and for treatment of certain malignant neoplasms such as lymphosarcomas, by using immobilized asparaginase. In clinical medicine, different types of bandages and tampons coated with immobilized enzymes are used. These enzymes are also contained in antibiotics, antiseptics and other drug preparations.

Immobilized drug agents, combined with various natural and synthetic polymers not only increase the hydrolytic resistance of these compounds but also increase the effectiveness of these drugs. The methods for immobilization make possible the production of drug preparations with complex effect by the process of combined immobilization (co-immobilization) of enzymes, antibiotics, hormones and other compounds which have markedly effective therapeutic properties. Studies conducted at the First Leningrad Medical Institute showed that the methods of radical co-polymerization and synthesis of water-soluble medicinal (co) polymers--vinylamin, vinylpyrrolidyl, ethenol and acrylic acid of predetermined composition and structure--can be utilized effectively in the production of such preparations.

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With the use of immobilized preparations, more exact and economical methods have been developed for mass clinical analysis to determine glucose, lactic acid and insulin levels in the blood, urea in serum, lactose in urine, penicillin in pharmaceutical preparations. The number of publications, related to the production and application of immobilized preparations in medicine grows every year. This attests to the importance of the problem of synthesis and use of such preparations in theoretical and clinical medicine.

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UDC 57:53(2.5);577.3.01;539.1y04;615.1

ANTIOXIDANT-ASSISTED CELL RECOVERY FROM RADIATION INJURY, AND THE RELIABILITY OF BIOLOGICAL SYSTEMS

Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 254, No 3, 1980 pp 760-762

[Article by V. K. Kol'tover, Yu. A. Kutlakhmedov, and Ye. L. Afanas'yeva, Chernogolovka Department of the USSR Academy of Sciences Institute of Chemical Physics, Moscow Oblast, and the Ukrainian SSR Academy of Sciences Institute of Plant Physiology, Kiev]

[Text] The viability of cells and multicellular organisms depends on the functional reliability of systems protecting subcellular structures and cells from spontaneous and induced injuries, and assisting in their recovery (1). Enzymatic systems assisting in the recovery (repair) of genetic structures play a special role (2). One quick reliability testing method used in engineering involves the testing of a system at heightened loads (3). Exposure to ionizing radiation followed by analysis of postradiational recovery of cells and tissues, during which the intensity of failures rises dramatically and the functional load upon protective and recovery systems rises, could be viewed as an analog of this method in biology. Let us assume that cells capable of limitless reproduction--that is, capable of forming macrocolonies in nutrient agar--are normally functioning cells. The cell survivability, defined as the ratio of the number of macrocolonies formed by irradiated cells to the number of macrocolonies formed by control cells, could serve as a statistical measure of cell reliability (probability of faultless function). The dependencies of survivability on radiation doses are analogous to the dependencies of equipment reliability on operating time, since the radiation dose rate corresponds to the intensity of failures arising during irradiation. These primary failures are a highly simple (Poisson) succession of random events, which simplifies mathematical analysis of the consequences of irradiation. In the rigid conditions of postradiational recovery, the positive or negative effects of physiologically active substances, to include various environmental factors that directly or indirectly alter the reliability of cells and tissues, should manifest themselves distinctly.

We studied the influence of 2-ethyl-6-methyl-3-oxypyridine chlorhydrate (alkyl-substituted oxypyridine, or AOP) on postradiational recovery of γ -irradiated diploid Megri 139-B *Saccharomyces ellipsoideus* (vini) yeast cells. This antioxidant was found to be an effective radioprotector (4) and geroprotector (5) in experiments on laboratory animals. The phenomenology of postradiational recovery of Megri 139-B cells has been studied well, the recovery process is extended in

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time, and it is easily modified (6, 7); this is why we selected precisely this strain as the system to model. Cells grown on beef-extract agar at 30°C until the late logarithmic phase were resuspended in sterile tap water at a concentration of 10^5 cells/ml and irradiated with an 800 Gr dose of ^{60}Co γ -quanta at a dose rate of 0.028 Gr/sec. To determine the recovery genetics, the irradiated cells were incubated at 30°C in the same water. They were periodically seeded on standard nutrient medium in Petri dishes, and survivability was determined by counting the macro-colonies (6). The experiments were performed with a fivefold replication. The results were treated according to a four-factor plan (8) having the radiation dose (0 or 800 Gr), the moment of addition of AOP to the medium (before or after irradiation), the AOP concentration, and recovery time as the factors. The mobility of membrane lipids was assessed by the spin probe method (9) using 6-doxylpalmitic acid as the probe. The probe's EPR spectrum was recorded at $25 \pm 1^\circ\text{C}$ with a Ye-104 spectrometer.

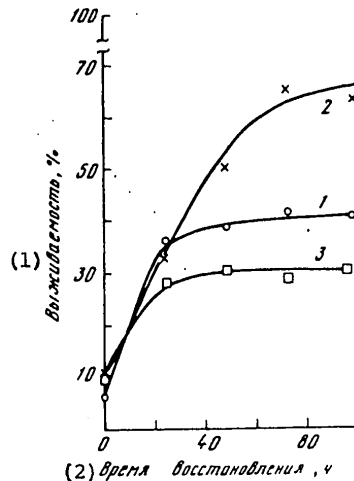


Figure 1. Typical Kinetic Curves of Postradiational Recovery of γ -Irradiated Yeast Cells With No AOP in the Recovery Medium (1), With 10^{-7} M AOP Introduced Into the Medium Before Irradiation (2), and With 10^{-3} M AOP Introduced Into the Medium After Irradiation (3)

Key:

1. Survivability, %
2. Recovery time, hr

Survivability of cells transferred to agar immediately after irradiation does not exceed a few percent (Figure 1). In this case most cells do not have enough time to repair damaged genetic structures before the onset of mitosis, resulting in formation of unviable daughter cells. Incubation in water containing no nutrients, in which the cells do not divide, affords additional time for repair processes to occur, and survivability increases correspondingly. In the presence of small AOP concentrations we observe a rise in the limiting values of survivability (a rise

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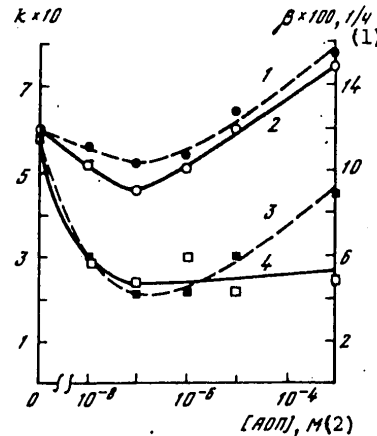


Figure 2. Proportion k of Irreversible Injuries (1,2) and Recovery Rate β (3,4) of γ -Irradiated Yeast Cells Depending on Concentration of AOP Introduced Into the Recovery Medium Before Irradiation (2,4) or After Irradiation (1,3); $\Delta k = \pm 0.04$, $\Delta \beta = \pm 0.008$ at $P = 0.05$

Key:

1. Hr
2. [AOP], M

in the plateau of the recovery curve), indicating a lower proportion of irreversible (irreparable) radiation injuries. Concurrently the rate of recovery declines. The kinetics of yeast cell recovery from radiation injury are described by a function of decreasing effective irradiation dose with time (6, 7):

$$(1) \quad D_{\text{eff}} = D_0 [k + (1 - k) \exp(-\beta t)],$$

where D_0 —irradiation dose, β —recovery rate (total probability of repair of elementary injury or its transformation into an irreversible form, per unit time), k —proportion of irreversible injuries. We used a standard curve describing the dependence of Megri 139-B cell survivability on dose to compute k and β (7). We can see from the dependencies of k and β on the AOP concentration, shown in Figure 2, that a preparation concentration of 10^{-7} reduces k by about 25 percent when introduced prior to irradiation, and by about 15 percent when added after irradiation. β varies symbatically with k . This confirms the hypothesis that irreversible injuries are the result of errors made by enzymes responsible for repair (7). k can be interpreted as an indicator of the functional reliability of these enzymes: A value of $k = 0$ corresponds to absolute reliability, while $k = 1$ corresponds to absolute functional unreliability of the genetic structure recovery system.

Reduction of k in the presence of small AOP concentrations means a rise in the recovery system's reliability. It is possible that AOP (or a product of its metabolism) modifies primary radiation-caused defects and facilitates their recognition by repair enzymes. Reduction of β apparently promotes a decrease in the

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probability of errors made during recognition and recovery. Pyridoxine analogs, which include AOP, inhibit RNA-polymerase in other enzymes dependent on pyridoxal-phosphate (10). Inhibition of such enzymes may cause a delay in cell division, and thus insure additional time for recovery of damaged genetic structures.

In concentrations exceeding 10^{-6} M, AOP increases k (Figure 2) and noticeably inhibits cells reproduction. The orderliness parameter (9) of the 6-doxalpalmitic acid spin probe in the membranes of intact cells decreases in the presence of 10^{-3} M AOP from 0.624 ± 0.004 to 0.605 ± 0.004 , indicating growth in the mobility of the hydrocarbon chains of membrane lipids. It may be concluded that at least at large concentrations, AOP has an effect on the structure of cell membranes.

At high irradiation doses the initial segments of the recovery curves can be approximately described by the expression:

$$(2) \quad S(t) - S(0) \approx nVD_0(1-k)[1 - \exp(-\beta t)],$$

which is easy to obtain from the dependence of Megri 139-B cell survivability on dose (6, 7) and expression (1) (n --extrapolation number, V --effective target volume). For the standpoint of reliability theory this means that elementary acts of recovery performed by repair enzymes make up, at the beginning of the process, a highly simple succession of random events with intensity β . The right side of (2) represents the probability that the process would be completed in time t , while the factor in front of the bracket represents the effectiveness of the elementary act of recovery. Deviation of the kinetics from expression (2) at large t may be associated with disturbance of stable conditions and mutual independence of elementary acts of recovery.

We note in conclusion that the universality of the postradiational recovery phenomenon permits use of the suggested approach to test the reliability of arbitrary biosystems, and to test the radioprotective, geroprotective, and anti-mutagenic properties of physiologically active compounds.

The authors are grateful to Academician N. M. Emanuel' and Ukrainian SSR Academy of Sciences Corresponding Member D. M. Grodzinskiy for their constant attention to the work, and to Prof Yu. K. Kapul'tsevich for his valuable advice in the work's discussion.

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PROTON MAGNETIC RELAXATION IN THE STUDY OF BURN PATHOLOGY DEVELOPMENT

Moscow DOKLADY AKADEMII NAUK SSSR in Russian Vol 254, No 3, 1980 pp 763-765

[Article by L. I. Murza, A. I. Sergeyev, V. I. Naydich, L. S., Yevseyenko, V. V. Disvetova, and T. V. Bunto, USSR Academy of Sciences Institute of Chemical Physics, Moscow]

[Text] The times of proton magnetic relaxation in biological cells and tissues are a basic characteristic of the mobility of water molecules. It was demonstrated earlier that relaxation characteristics are associated with the concentration of water in these biological objects (1, 2). Up to the present, the proton magnetic relaxation method had been used in experimental and clinical medicine mainly to study tumorous growth (2-4). However, changes in relaxation times may also characterize other pathological processes associated with accumulation of water in tissues (edema). This paper is a study of change in the time of proton spin-lattice relaxation, T_1 , in animal tissues during development of experimental burn pathology.

The experiment was conducted on mongrel male rats weighing about 120 gm. The side of the haunch (4-6 percent of the body surface area) was shaved and then exposed to 95-100°C water for 20 seconds. This produced IIIA-IIIB degree burns, edema, formation of a scar followed by rejection of some skin, and an inflammatory reaction in muscle tissue in the muscle area subjected to thermal trauma; no necrosis occurred. During the experiment the animals were afforded an unrestricted drinking regimen.

The kinetics of change in the time of spin-lattice relaxation in scalded skin and muscle tissue in the burn area, and in organs not directly subjected to burn trauma--the liver, kidneys, spleen, brain, and blood--were studied. Tissue samples (100-120 mg) were taken for analysis immediately following asphyxiation, bled on filter paper, and placed in the working vial of a spectrometer. Measurements were made at $30 \pm 1^\circ\text{C}$ for 1 hour following sample preparation. It was established that the relaxational characteristics of tissues do not change during this time.

The time of proton relaxation was measured with a "Minispek r-20" pulse spectrometer made by the East German "Bruker" company, having an operating frequency of 20 MHz. A two-pulse sequence, $90^\circ-\tau-90^\circ$, was employed for the measurements. Each experimental point on the kinetic curves required tissue samples from five or six animals. The graphs show the mean values of T_1 and the standard deviations.

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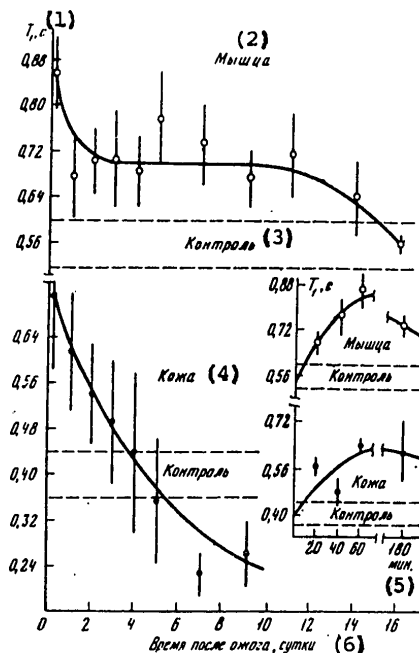


Figure 1. Time of Tissue Spin-Lattice Relaxation Following Experimental Burn Injury: Inset shows the initial period of the process

Key:

- | | |
|------------|---------------------------------|
| 1. Sec | 4. Skin |
| 2. Muscle | 5. Min |
| 3. Control | 6. Time after burn injury, days |

Figure 1 shows the kinetic curves for change in T_1 in samples of skin and muscle tissue from the burn area. Changes in capillary permeability and diffusion of blood plasma from vessels into injured tissues caused tissue edema (5, 6)--that is, an increase in water, which apparently is responsible for the increase in T_1 . Within 1 hour, the relaxation time of dermal tissue rises by a factor of 1.5, and after reaching a maximum, it begins to fall as the injured area dries out and a scar forms.

Relaxation time increases almost as quickly in scalded muscle tissue. It is commonly known that pathomorphological changes and visible muscle injury are not observed with III degree burns. Nevertheless the relaxation time of muscle tissue remains high for a long period of time following burn injury.

Figure 2 shows the nature of change of T_1 in liver and kidney tissues--that is, in tissues not directly exposed to thermal injury. In both cases we observe significant growth in relaxation time, which is apparently associated with an increase in tissue water. Change in T_1 in the liver may be a product of higher permeability of

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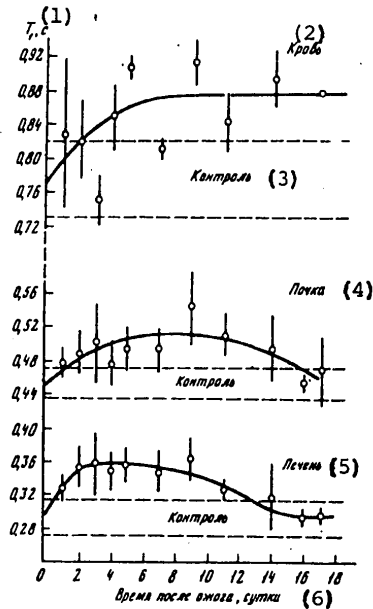


Figure 2. Time of Spin-Lattice Relaxation of Tissues Not Subjected to Direct Burn Injury

Key:

- | | |
|------------|---------------------------------|
| 1. Sec. | 4. Kidney |
| 2. Blood | 5. Liver |
| 3. Control | 6. Time after burn injury, days |

vessel membranes (5, 7). The function played by kidneys in the water-electrolyte balance may be another factor influencing change in the relaxation time of kidney tissue, since published data indicate significant changes in this balance in response to burn injury (5). Growth in T_1 in liver and kidney tissue continues beyond the 1st day, even after the animals recover from shock. The time of higher T_1 values obviously coincides with the period of burn toxemia. This permits the hypothesis that the increase in time of spin-lattice relaxation is not associated with shock, being instead the result of action of burn toxins upon the body (5, 8).

It is commonly accepted that burn disease arises over more than 10 percent of the body surface area with IIIA-IIIB degree burns (8). We discovered change in relaxation characteristics in response to significantly lesser thermal influence (a burn area of about 5 percent). This change was observed in organs remote from the burn area, and obviously it reflects the state of the body as a whole. Thus we may hypothesize that burn disease can also arise when the injured area is small; this should be considered when treating burn victims.

Inasmuch as plasma loss and disturbance of tissue metabolism promote blood coagulation (6), we would have expected a decrease in T_1 in blood during the initial phase of burn development. However, changes in blood relaxation time were not

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revealed by our experiments in this phase, and as the burn process developed, a certain increase in the blood T_1 was recorded (Figure 2).

Plethora and edema of the brain and brain membranes are invariable signs observed in victims dying in the burn shock stage (8); thus we were highly interested in measuring T_1 in brain tissues. However, no changes were observed in the brain with the burn surface area employed here.

The results permit the conclusion that it would be suitable to study the processes of experimental burn pathology with the help of the magnetic relaxation method. This method reveals subtler changes in tissue subjected to thermal injury than does conventional morphological analysis. Changes not clinically observable are revealed at the organismic level. This may make it possible to develop more-precise criteria for optimum treatment of burn disease. Clinical application of the method as a means for keeping pathological development and therapeutic effectiveness under observation is beginning to show promise in connection with development of ways to measure the relaxation characteristics of tissues *in vivo*, without their dissection (9, 10).

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STRUCTURAL-FUNCTIONAL ASPECTS OF NEUROPHYSIOLOGY

Leningrad STRUKTURNO-FUNKTSIONAL'NYE ASPEKTY NEYROFIZIOLOGII in Russian 1978 signed to press 22 Mar 78 pp 227-231

[Table of contents from a collection of papers from the Conference of Young Scientists and Specialists, Scientific Council on Complex Problems of the Physiology of Man and Animals, USSR Academy of Sciences, 500 copies, 231 pages]

[Text]

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UDC 616.127-005.8-06:616-001.36-092.9-001.57

CARDIOGENIC REFLEXES AND THEIR ROLE IN THE REGULATION OF BLOOD CIRCULATION

Kiev KARDIOGENNYYE REFLEKSY I IKH ROL' V REGULYATSII KROVOOBRAASHCHENIYA in Russian
1979 signed to press 9 Oct 79 pp 2-6, 262-263

[Annotation, introduction and table of contents from book "Cardiogenic Reflexes and Their Role in the Regulation of Blood Circulation", by A. A. Moyenko, A. A. Bogomollets Institute of Physiology, UkSSR Academy of Sciences, Izdatel'stvo "Naukova dumka", 2100 copies, 264 pp]

[Text] This monograph presents bibliographical data and the results of the author's research on the nature of the heart's receptivity and the role of the reflexes of the various receptor zones of the heart in the regulation of blood circulation under normal conditions and during ischemia of the myocardium. It is found that cardiogenic reflexes have great potential significance in the regulation of blood circulation and that they play a primary role in the regulation of the activities of the heart itself. It is established that the receptor zones of the left and right hemispheres of the heart are functionally different and that the receptors of the left ventricle are of primary significance in the regulation of vascular tonus of the larger circulatory area. It is shown that changes in the contraction activity of the myocardium and vasomotor reactions are reflex-interrelated.

The present state of reflex regulation of blood circulation research is characterized by a tendency away from purely analytical studies toward the synthesis of obtained data with the goal of developing the basic principles which govern blood circulation. This is related to the accumulation of factual material on the reflex regulation of hemodynamics, the activity of the heart and the vascular tonus, the development of research on the central regulation of blood circulation and the application of new analytical methods to experimental data. This direction in research has extraordinary significance in the development of the problem since it generalizes the most valuable results obtained by various researchers, indicates the direction and perspective of further research and at the same time it expresses and emphasizes the incompleteness and lack of factual data as well as of our model of the mechanisms of reflex regulation of blood circulation.

In analyzing factual material on the reflexes of the cardiovascular system it is impossible not to note that individual reflexogenic zones of the cardio-vascular system are not equally well studied. This is especially true of research on the reflex reactions from these zones to adequate stimuli.

Almost all of the data on the most important parameters of the function of receptor zones of the circulatory system (the threshold for the appearance of the reflex, maximum sensitivity, regulatory limits) is obtained on the basis of sinocarotid reflexogenic zones. The basic data on this problem is given in the works of Koch (1931),

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Heymans and Neil (1958), N. N. Gorev (1959), V. M. Khayutina (1964), Korner (1971), Folkow and Neil (1971), Abboud et al (1976) and others. Corresponding data on the function of the receptor zone of the arc of the aorta are less numerous, while the receptor field of the heart in this respect is practically not studied. The significant majority of data on the effect stimuli on the receptor zones have on the contracting function of the myocardium, the cardiac ejection and the regional vascular resistance is also related to the sinocarotid zone.

The insufficient data on the physiological reality of reflex reactions which are generated from different receptor zones, on the conditions of their inclusion in adapting circulatory reactions and on the specifics of their effector structures, on their relative physiological significance as well as on the character and mechanism of the interactions of the various afferent apertures is one of the major obstacles to formulating sound conceptions about the principles of the reflex regulation of blood circulation. Obviously, it is precisely these conditions which nurture the unfailing and recently increased interest of the researchers in the problem of the receptivity of the heart (Frol'kis, 1952, 1959; Kulayev 1954, 1972; Chernigovskiy 1960; Trubetskoy 1961; Tkachenko et al, 1964, 1975; Khomazyuk et al, 1965, 1969; Udel'nov et al, 1966, 1975; Kositskiy et al, 1965, 1975; Khayutin et al, 1970; Oberg et al, 1968, 1976; Brown et al, 1964, 1971; Malliani et al, 1969, 1977, and others).

The reflexogenic field of the heart occupies a special place in the reflex regulation of circulation, which is determined by a series of anatomical and functional factors. Especially important is the fact that the heart receptors are located in the central organ of the circulatory system, locked within the heart muscle with a constantly changing work regime, whose level in turn is regulated by nervous and humoral factors. Therefore, afferentation which comes from the reflexogenic field of the heart can be realized in the changing function of the heart itself, being within the limits of reflex regulation as a cardiocardial reflex with a closure of reflex arcs at various levels of the central nervous system, and, obviously, in the heart itself (Udel'nov, 1968, 1975; Kositskiy, Chervova 1968).

The second, no less important, factor is that the heart is a very large receptor field, whose zones are distributed among its various parts with individual functional characteristics. The left and right halves of the heart function with a different degree of diastolic dilatation and resistance load, a different level of metabolic processes. Therefore, it can be supposed that the stimuli conditions of the receptors and the functional significance of the reflexes from various parts of the heart can have real differences.

And finally, the third characteristic of the reflexogenic field of the heart, which to a significant degree complicates the task of studying it, consists of the fact that the heart is a part of a general system of innervations of the organs in the chest cavity. All extracardiac "heart nerves" innervate not only the heart but also its surrounding organs and tissues. In addition, afferent and efferent heart nerves are intimately intertwined from their emergence from the central nervous system to the innervating substratum.

These characteristics of the reflexogenic field of the heart in totality result in extraordinarily great difficulties for experimental study and require the application of special methodological tools.

In spite of the fact that the possibility of reflex reactions from the receptor field of the heart was already described in the work of Bezolid and Hirt (1867) and conclusively proven in the works of Jarisch and Richter (1939a, 1939b), the potential significance of reflexes from the heart in the regulation of circulation has not yet

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been determined. Data on the changes of cardiac ejection during reflexes from the heart and on the change in the contraction function of the myocardium are terribly insufficient or lacking; the information on the regional vascular reactions is fairly contradictory.

Studies on comparative characteristics of the hemodynamic and vasomotor reactions during cardiogenic reflexes and other particular reflexes of the circulatory system are almost non-existent.

These conditions determine the first task of our researchers--the study of the effector structure of the cardiogenic reflexes and the explanation of their potential significance in the regulation of circulation. Among these are included studies on the reflex changes in cardiodynamics and in the contracting function of the myocardium; the reflex shift of the basic hemodynamic parameters (cardiac ejection, systematic arterial pressure, general peripheral resistance) and the regional vasomotor reactions in large and small circulatory areas, as well as a comparative evaluation of the reactions of the cardiovascular system to cardiogenic and sinocarotidic reflexes.

The results of a great majority of morphological and electrophysiological studies (Lavrentyev 1927; Hirsch 1947, 1964; Plechkova 1948, 1968; Paintal 1953, 1973, 1977; Coleridge et al, 1957, 1973; Khabarova 1961, Seto 1963; Gilev 1963, 1964; Yasinovskaya 1964, 1973; Kulayev 1965, 1966; Gilev, Kurilenko 1966; Abraham 1969, Thoren 1972, 1977, and others) do not leave any doubts that the powerful and varied receptor apparatus of the heart sharply reacts to cardiodynamic changes which are possible during the most diverse adapting reactions of the organisms. However, the position that the physiologically possible changes in the activity of the heart can lead to the appearance of expressed cardiogenic vasomotor reflexes is insufficiently proven. The very principle of including reflexes from the heart in the self-regulatory circulatory system remains unexplained; do the cardiogenic reflexes appear in response to changes in the metabolism of the myocardium or are the changes in cardio-mechanics the prime factors in their appearance? What precise changes in the heart regime (an increase in the hyperemia of the cavities, an increase in the contractibility of the myocardium) are most important in the appearance of the cardio-cardial and cardio-vascular reflexes. Our research on the cardiogenic reflexes which appear when physiologically active substances act on the receptor zones of the heart and during changes in the work regime of various parts of the heart is motivated by the desire to obtain answers to these questions.

The author wishes to express his gratitude to the coworkers of the experimental cardiology section of the A. A. Bogomolets Institute of Physiology of the Academy of Sciences of the Ukrainian SSR for their cooperation in conducting experimental studies and expresses his sincere indebtedness to Academician N. N. Gorev of the Academy of Medical Sciences of the USSR for his constant help.

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ENVIRONMENTAL HAZARDS

INFORMATIONAL MACROMOLECULES IN RADIATION DISTURBANCES OF CELLS

Moscow INFORMATSIONNYYE MAKROMOLEKULY PRI LUCHEVOM PORAZHENII KLETOK in Russian 1980 signed to press 4 Mar 80 pp 2-5, 174-175

[Annotation, introduction and table of contents from book "Informational Macromolecules in Radiation Disturbances of Cells", by V.Ye. Komar and K.P. Khanson, Atomizdat, 1200 copies, 176 pages]

[Text] Current data on the structure and functional activity of informational macromolecules in response to radiation disturbances of cells are discussed in this book. The results of multiple studies concerning the effect of ionizing radiation on the structure and biosynthesis of DNA and transcription and translation of genetic information are presented. The role of disturbances of the informational apparatus in the mechanism of reproduction and interphasic death is examined. Data are presented on the function of the internuclear genetic apparatus in response to radiation disorders.

This book, discussing some interesting questions on molecular radiobiology, is relevant to the work of radiobiologists, physician radiologists as well as specialists in other areas. 46 diagrams; 8 tables; 316 references.

Introduction [by professor Ye. F. Romantsev, corresponding member of the USSR Academy of Medical Sciences]
Examination of the molecular bases of the effect of ionizing radiation on biologic objects is one of the fastest growing areas in modern radiobiologic research. The rapid accumulation of new information on this problem has led to the need for publication of review volumes and monographs related to various aspects of molecular radiobiology.

In its second edition, this book authored by V. Ye. Komar and K.P. Khanson presents a compendium of current data on the

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structure and function of informational macromolecules given radiation disturbances mainly of cells in higher organisms. The book presents to a greater or lesser extent, all the basic problems of molecular radiobiology. Current data on the nature and mechanisms of damage to the genome as a result of exposure to ionizing radiation are presented. Also discussed are the molecular mechanisms which protect the cell from damage. Based on their own and data found in the literature, a detailed analysis of the effect of radiation on the biosynthesis of DNA and on transcription and translation of genetic information is presented.

Chapter 1 is a very concise and useful discussion of the basic principles of function of the system of informational macromolecules. Their discussion adds significantly to understanding this material. The authors present very complete reflections of the newest achievements in molecular radiobiology which have served to clarify the chemical nature of damage to DNA in the cells, the molecular mechanisms to protect the genome from damage, the mechanisms to suppress by use of radiation the biosynthesis of DNA and the significance of this phenomenon in the post-radiational state of the cells. Multiple studies by a number of laboratories on the process of transcription in irradiated cells are discussed.

Data on the effect of ionizing radiation on the informational macromolecule in the mitochondria are reviewed for the first time. The authors' various theories on the molecular mechanisms of interphasic death in lymphoid cells are presented in chapter 8. This form of cellular death to a significant degree, determines the nature of the radiation induced disease but the mechanisms which form the basis of interphasic death and the role of the informational macromolecule in this process is characteristic for this cellular population.

The authors utilize a broad representation of native and foreign literature concerned with the effect of radiation on the system of the informational macromolecule and also their own experimental data.

The book is written on a high scientific level, is well illustrated and, without doubt, will be valuable for all scientific workers concerned with the problems of molecular radiobiology.

Authors' Introduction

After the publication of the first edition of this book (1972) a large number of new facts on molecular radiobiology have been accumulated which require interpretation and review. In this book, we attempted to shed light on current concepts of the effect

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of ionizing radiation on various components of the system of informational macromolecules in living cells. With a few exceptions, the text of this edition has been rewritten.

Questions which we examine have been carefully selected and we have re-examined the scope of individual chapters identifying those areas in which the most progress has been made. We excluded the chapter on molecular mechanisms of radiosensitivity of cells. The interested reader can find a detailed review of this topic in the book entitled: "The Limits of the Modification Process Produced by Radiation Disturbances" (Atomizdat, 1978), edited by P.G. Zhrebchenko and A.V. Savich. We expanded significantly sections dealing with questions on the study of the structural damage to the DNA molecules and their post-radiational repair as well as studies on the extra-nuclear (mitochondrial) genetic system and interphasic cellular death.

Considering the recent achievements in molecular biology and the enormous influence which the field has exerted on radiobiology, we felt it necessary to write a special introductory chapter concerning current data on the functional principles of the informational apparatus of cells. Naturally, we tried to present only the most important facts. Nevertheless, we assume that the material presented will encompass the main elements of current radiobiologic data.

In conclusion, we emphasize that radiobiologic studies now have special importance because of the constantly expanding sphere of use of ionizing radiation in agriculture, medicine and science. A wide range of information on the different aspects of radiobiology has been accumulated. However, the basic mechanisms of the biologic effect of radiation remain, to a significant degree, undeciphered.

We will consider our task complete if this analysis of the function of informational macromolecules in irradiated cells helps progress in this difficult area.

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UDC 612.015.3:546.79:577.391:614.876] 519.9

ABSTRACTS FROM THE COLLECTION 'SIMULATION OF THE BEHAVIOR AND TOXIC EFFECTS OF RADIONUCLIDES'

Sverdlovsk MODELIROVANIYE POVEDENIYA I TOKSICHESKOGO DEYSTVIYA RADIONUKLIDOV in Russian 1978 pp 2, 99-104

[Annotation and abstracts from the collection edited by Ye. I. Sukhacheva, Ural Scientific Center of the USSR Academy of Sciences]

[Text] This collection presents the data on the regularities of toxic effects of radioactive isotopes on individual systems and on the entire organism in normal and extreme conditions. Mathematical simulation methods are used to evaluate the toxic effects of radioisotopes, and problems of the pharmacodynamics of certain complex-forming preparations are examined. Possibilities of the extrapolation of the obtained data from animals to man are discussed. A number of articles treat the mechanisms of the distribution of radioactive metals, the effects of biosubstrata on the exchange of isotopes in the organism, and the physicochemical state of radiators in the blood. The collection is intended for radio biologists, biochemists, toxicologists, biophysicists, pharmacologists, and physiologists.

UDC 615.849.2:546.641:612.35:615.015.25

AN ATTEMPT TO ELIMINATE YTTRIUM-91 FROM THE LIVER BY THE EDTA COMPLEXING SUBSTANCE

[Abstract of article by A. V. Bazhenov]

[Text] It is shown on the perfusing liver of rats that, after 24 hours of its treatment with yttrium-91, EDTA [ethylenediaminetetraacetate] does not wash out the radiator. The elimination of the metal occurs through the bioligands of the blood. Tables -- 1, bibliography -- 5 items.

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COMPETITIVE RELATIONS BETWEEN YTTRIUM AND BROMSULPHALEIN FOR ACCUMULATION
IN THE LIVER AFFECTED BY CCl₄

[Abstract of article by A. V. Bazhenov]

[Text] The author shows in model experiments, i.e., under the effect of carbon tetrachloride and with the blocking of the liver by bromsulphalein, that there exists competition for the absorption of bromsulphalein and yttrium-91 by the liver; parenchymal cells take a considerable part in this process. Bibliography -- 5 items.

UDC 612.015.3:621.039.85:615.099.08:546.815:519.9

MATHEMATICAL SIMULATION OF LEAD METABOLISM AFTER ITS SINGLE AND REPEATED
ADMINISTRATION TO RATS

[Abstract of article by V. S. Bezel']

[Text] The author examines the metabolism of lead in the organisms of rats. Individual chambers are isolated in the model: the blood and some internal organs, muscles and the skin, the liver and kidneys, and the skeleton. The parameters of the model were determined by the experimental data for a single intravenous administration of lead nitrate-210. Two kinetically different pools of the metal were isolated in the skeleton, muscles, and the skin of the animals. In the rapid-metabolism fraction of the metal in the skeleton, the maximum amount of lead was observed on the second day after administration. By the 25th-30th day, there forms a weak-metabolism depot, from which the liberation of metal into the blood chamber is characterized by a very low intensity. In the muscles and in the skin, about ten percent of the original content of the metal is fixed in the form of a strongly bound fraction. The excretion of lead with the feces occurs chiefly through its elimination into the intestines with the bile (up to 80 percent). One third or one fourth of the amount is eliminated with the urine, chiefly, due to the secretion in the tubules of the kidneys. When repeated administration of lead was simulated on the model, the levels of the metal content in the skeleton and the daily elimination with the feces differed somewhat from the corresponding experimental data. This difference could be caused by the "weightiness" effect of the metal which was observed in the fluids of the organism during repeated administrations. Figures -- 4, bibliography -- 12 items.

UDC 612.015.3:612.4.44:546.47:615.015.25

THE ROLE OF THE ENDOCRINE SYSTEM OF CALCIUM METABOLISM IN THE ELIMINATION
OF ZINC BY A COMPLEXING SUBSTANCE

[Abstract of article by N. M. Lyubashevskiy, V. S. Bezel', B. V. Popov, and M. N. Belova]

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[Text] It is shown that the sodium form of EDTA is more effective in the elimination of zinc from the organism than the calcium form; the effectiveness of both forms of EDTA is identical in thyreo-parathyrosialoectomized animals deprived of the endocrinic regulation of calcium metabolism. The sodium form of the complex-forming substance has an additional effect of triggering the endocrinic mechanism. The latter increases the resorption of the bone and the removal of additional amounts of the metal contained in the skeleton into the blood. Tables -- 3, bibliography -- 7 items.

UDC 612.015:3546.641:621.039.85:591.471.3

ANALYSIS OF THE SORPTION AND DESORPTION BY TISSUES OF COMPLEX AND SIMPLE SALTS OF YTTRIUM-91 IN EXPERIMENTS ON PERFUSING LIMBS

[Abstract of article by N. M. Lyubashevskiy and S. S. Lekokhmakher]

[Text] The authors conducted experiments on perfusing limbs of rats to study the delay of radioactive markers during the perfusion of solutions of ⁹¹Y-EDTA, ⁹¹Y-NTA, ⁹¹Y-citrate, and weighable and unweighable concentrations of yttrium chloride. The permeability of the capillary wall for the studied compounds was evaluated by the degree of the accumulation of the radioisotope. The strength of the fixation by the tissues was determined by the degree of its washing-off by the blood-substituting fluid (polyglucinum) and by the EDTA solution. Tables -- 2, figures -- 1, bibliography -- 6 items.

UDC 615.015.13:541.49:615.015.3:546.47:519.9

THE USE OF A MATHEMATICAL MODEL OF ZINC METABOLISM IN STUDYING THE TOXICITY OF COMPLEX-FORMING SUBSTANCES

[Abstract of article by B. V. Popov and V. S. Bezel']

[Text] A mathematical model of zinc metabolism was used to calculate the dynamics of the content of this element in individual organs and tissues of albino laboratory rats under the effect of four different modes of introduction of the complex-forming substance Ca-DTPA [diethylenetriaminopentaacetic acid] in doses corresponding to cumulative LD_{50/30} for each mode. It is shown that under certain conditions there exists a close correlation between the toxic effect of the complex-forming substance and the zinc level in the organs and tissues of rats. Figures -- 3, bibliography -- 12 items.

UDC 612.015.3:612.352:546.641:547.962.3

INVESTIGATION OF THE ROLE OF ALBUMIN IN THE DISTRIBUTION OF YTTRIUM-91 IN THE ORGANISM

[Abstract of article by D. I. Semenov, Ye. I. Sukhacheva, N. M. Lyubashevskiy, T. P. Arkhipova, and A. P. Il'inykh]

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[Text] The authors studied the effects of serum albumin on the behavior of radioactive yttrium in the organisms of rats under various weight amounts of the isotope carrier and a constant dose of protein in the injected solutions in intact rats and rats affected by silicosis with disturbances in the protein metabolism. The yttrium-protein ratios in the solutions were $2 \cdot 10^{-6}:1$; $0.02:1$; $0.2:1$; $2:1$; $20:1$. The animals were killed twenty four hours after the administration of the solution. For most tissues, the distribution of yttrium-91 and labeled protein was identical, which is an indication of the transport role of albumin. In the rats affected by silicosis, the level of the deposits of labeled protein in the liver decreased sharply, which resulted in a decrease in the deposits of radioactive yttrium in this organ. It is shown that yttrium cations have a marked effect on the albumin metabolism. Tables -- 3, figures -- 3, bibliography -- 9 items.

UDC 541:546.641/541.8:547.96

INTERACTION OF MICROAMOUNTS OF YTTRIUM WITH SERUM PROTEINS

[Abstract of article by N. V. Mikshevich, D. I. Semenov, Yu. V. Yegorov, and V. V. Kuptsova]

[Text] Methods of ion exchange, foam chromatography, and gel filtration were used to study the state of microamounts of yttrium in solutions of serum proteins. It was shown in experiments in vitro and in vivo that the formation of yttrium complexes with the studied proteins begins at $\text{pH} > 3$ and in a weak acid medium progresses with the participation of exchange processes. In the area of physiological pH, apart from the participation in the reactions of complex formation, the authors observed the possibility of the formation of microcomponents as a result of the hydrolysis of complex-nature colloids. The stability of the complex compounds of yttrium with proteins in the area of physiological pH increases in the series: albumin $<$ alpha-globulin $<$ native serum. Figures -- 3, bibliography -- 31 items.

UDC 577.39:614.876:546.36/42

THE CONTENT OF STRONTIUM-90 AND CESIUM-137 IN AGRICULTURAL PRODUCTS OBTAINED AT PUBLIC AND INDIVIDUAL FARMS

[Abstract of article by A. M. Skryabin and Z. A. Permikina]

[Text] The authors studied the effects of the methods of conducting agricultural production on the rate of the contamination of milk and potato by long-lived radionuclides. Under the conditions of global radioactive contamination, the concentration of strontium-90 and cesium-137 in milk and potatoes produced in the individual sector in rural areas is higher than in the public sector. This is connected with the special characteristics of feeding the livestock at the two types of farms. On this basis, it is proposed to evaluate differentially the intake of radionuclides and radiation doses for different groups of rural population.

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UDC 577.39:614.876:546.42

EXPERIMENTAL STUDIES ON THE DISTRIBUTION OF STRONTIUM-90 OVER THE CROSS
SECTION OF CERTAIN TYPES OF SOILS

[Abstract of article by Ye. I. Belova and A. Ya. Kogotkov]

[Text] The authors present the results of experimental studies under natural conditions on the distribution of strontium-90 over the cross section of soils and evaluate the parameters of a migration model on the basis of these studies. Studies were conducted in the course of twelve years on three types of soils. In the course of 5-6 years after the introduction of the isotope, the distribution over the cross section of the soils followed the exponential law. After 5-6 years, the maximum content of the isotope moved to deeper strata. The authors obtained the parameters of a semiempirical model of strontium-90 migration in soils which were used for predicting the content of this isotope in the root-containing strata of three types of soils in the interval of 0-60 years for a single introduction of the isotope. Tables -- 3, figures -- 1, bibliography -- 8 items.

UDC 577.39:614.876:546.36/42

ON THE INTERACTION MECHANISM OF RADIOACTIVE ISOTOPES OF STRONTIUM-90 AND
CESIUM-137 WITH THE SOIL

[Abstract of article by R. I. Pogodin and E. A. Polyakova]

[Text] The authors presented the results of studies on the effects of the time of contact of strontium-90 and cesium-137, the structure of the absorbing complex of the soil, and the content of chemical analogs in the soil on the migration ability and biological accessibility of the isotopes in the soil system. Figures -- 2.

UDC 577.39:614.876:546.36:661.84

DIFFERENTIAL DISLODGEEMENT OF CESIUM-137 FROM MINERALS AND SOILS WITH POTAS-
SIUM FERROCYANIDE SOL

[Abstract of article by G. Ye. Sharonov and R. I. Pogodin]

[Text] The article gives the results of studies on the applicability of potassium ferrocyanide sol for determining the mobility and content of exchange cesium-137 in soils and minerals. Tables -- 1, figures-1, bibliography -- 3 items.

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UDC 577.39:621.039.76:519.9

SIMULATION OF THE GAMMA-RADIATION FIELD OF A WATER RESERVOIR UNDER LABORATORY CONDITIONS

[Abstract of article by V. A. Baturin and I. Ye. Konstantinov]

[Text] The authors studied the dose characteristic of the gamma-field of an experimental water reservoir. The isotope of cesium-137 which is present in the water and is incorporated in the bottom deposits is responsible for the values of the dose rates from such a water reservoir. It is practically impossible to evaluate the share of the contribution of each of these sources to the dose rate. The existing calculation methods, for example, the Monte-Carlo method, are very laborious due to the presence of three components of the medium (water, air, soil) and the complexity of the geometry of the source and require an extremely great amount of the machine time. By using the method of simulating large sources under laboratory conditions, the authors obtained values of dose rates which are due to the activity of the isotope contained in water. The difference of the experimental total values of the dose rates from the water reservoir and the values obtained as a result of model studies (from water) makes it possible to evaluate the share of the contribution to the dose rate from the isotope incorporated in the bottom deposits. Figures -- 1, bibliography -- 3 items.

UDC 577.39:628.394:546.79

ON THE PROBLEM OF THE DISTRIBUTION OF CERTAIN LONG-LIVED RADIOACTIVE ELEMENTS IN A WATER RESERVOIR AND THEIR TRANSITION TO ICE

[Abstract of article by V. A. Baturin, I. G. Vodovozova, and L. N. Korchak]

[Text] The authors studied the distribution of a number of radioactive isotopes (strontium-90, cesium-137, cerium-144, ruthenium-106, cobalt-60) in various components of an experimental water reservoir (silt-water-ice). In the water-silt system, cesium-137 which is in the cation form has the highest sorption capacity ($K_d=320$), and cobalt-60 which is in the anion form has the lowest sorption capacity ($K_d=13$). Migration of radionuclides over the cross section of bottom deposits is described by exponential relations. The highest freezing effect is observed in cesium-137 (680) and the lowest in cerium-144 (10). Bibliography -- 9 items.

UDC 577.39:613.648:591.16

EFFECTS OF CHRONIC EXPOSURE OF THE PIKE (*Esox lucius* L) ON ITS REPRODUCTIVE FUNCTION

[Abstract of article by G. B. Pitkyanin]

[Text] The author gives the results of studies on the weight increase, fertility, and the quality of the offsprings of the pike which lived for a long time in an experimental water reservoir polluted by strontium-90 and cesium-137. The concentration of the pollutants exceeded the global levels by approximately five orders of magnitudes. The annual increase in the weight of the pike body from the experimental water reservoir was good, but the reproductive function was lowered, chiefly, due to an increase in deformities.

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among the offsprings which can be considered to be the result of the irradiation of the spawners' sections of the gonads adjacent to the walls of the intestines. Tables -- 1, figures -- 2, bibliography -- 6 items.

UDC 614.876:53.082.79

A SCANNING DEVICE FOR THE HUMAN-BODY RADIATION SPECTROMETER SICH-9.1

[Abstract of article by B. S. Zaytsev and V. P. Kozheurov]

[Text] This article describes a scanning device used in SICH-9.1. It is a tracking system and consists of a control unit and activating motors. The relocation law is set by replaceable program disks which are installed on the axis of the spacing drive controlled by pulses from the "live"-time timer of the analyzer. Provisions are made for changing the scanning time and regulating the path length. The error in the adjustment of the prescribed relocation law in the device does not exceed $\pm 1\%$. Figures -- 2, bibliography -- 3 items.

UDC 614.876:53.082.79

CALIBRATION OF THE HUMAN-BODY RADIATION SPECTROMETER SICH-9.1 FOR STRONTIUM-90

[Abstract of article by V. P. Kozheurov, L. I. Panteleyev, I. M. Rasin, and I. A. Sarapul'tsev]

[Text] The most objective information about the content of strontium-90 in a human organism can be obtained from direct bremsstrahlung measurements on SICH units. One of the problems in using this method is the calibration of the spectrometer. The authors discussed the calibration of the SICH-9.1 by the bremsstrahlung of strontium-90+yttrium-90 with the aid of a special anthropomorphic phantom with a natural human skeleton and soft tissues simulated with paraffin. Tables -- 1, figures -- 2, bibliography -- 9 items.

UDC 614.876:53.082.79

AN AUTOMATIC UNIT FOR INTRAVITAL REGISTRATION OF BETA-ACTIVE RADIOISOTOPES IN ANIMAL ORGANS AND TISSUES

[Abstract of article by V. A. Baturin and P. M. Malkin]

[Text] The authors describe the circuit of an automatic device consisting of standard electronic assemblies which is intended for simultaneous registration of the content of radioactive isotopes -- beta-emitters in the organs and tissues of large experimental animals. This unit makes it possible to shorten the time and the expenditure of animals, as well as to increase the accuracy of experiments on the kinetics of the exchange of beta-emitters in various organs and tissues of large experimental animals. Figures -- 1, bibliography -- 4 items.

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UDC 577.391:546.655.3:615.015.25

ACCESSIBILITY OF CERIUM-144 FOR DTPA

[Abstract of article by I. P. Tregubenko, G. A. Men'shikova, and D. I. Semenov]

[Text] Injection of Ca-DTPA increases sharply the elimination of cerium-144 with the urine and feces on the 3rd, 8th, 13th, and 18th day after the incorporation of the emitter. The increased elimination lasts for several days after the first injection; the effect of a repeated injection is considerably less marked. By administering 200 micromoles of DTPA three times in the course of the first two weeks, it is possible to eliminate about 30% of radiocerium above the 35% naturally eliminated with the urine and feces. The time changes in the DTPA effectiveness correlates well with the total cerium-144 content in the organism by the moment of the injection of the complex-forming substance. By repeated DTPA injections, it is possible to mobilize from the organism over 80% of the cerium-144 deposited in the tissues. Tables -- 2, figures -- 2, bibliography -- 9 items.

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UDC 577.3:539.12.04+539.125.52

HUMAN MODELING: DISTRIBUTION OF NEUTRON RADIATION

Moscow DOZOVAYA NAGRUZKA NA CHELOVEKA V POLYAKH GAMMA-NEYTRONNOGO IZLUCHENIYA in Russian 1978 signed to press 29 Dec 77 pp 2-4, 165-166

[Annotation, introduction and table of contents from book "Human Dosage Loading in Gamma-Neutron Radiation Fields", by V. L. Gozenbuk, I. B. Keirim-Markus, A. K. Savinskiy and Ye. N. Chernov, Atomizdat, 1500 copies, 166 pages]

[Text] The book deals with the tissue distribution of radiation dosage from an external gamma-neutron source in a model of the human body.

Consideration is given to the formation of a gamma-neutron emission field in nuclear reactor installations and at critical sites. The results of calculated tissue dosages in these fields are presented and analyzed. Special attention is accorded to calculation of dosage loads at critical organs and tissues. Recommendations are given for the use of computers in operative determination of probable sequelae of acute and chronic gamma-neutron irradiation.

The book makes it possible to evaluate the sequelae of gamma-neutron irradiation under various conditions.

The book is intended for workers in the dosimetry of external radiation, research radiobiologists, radiologists, and dosimetrists, as well as for fellows and students attending advanced courses with an interest in the theoretical and practical aspects of dosimetry.

Introduction

Nuclear energy and ionizing radiation are becoming common facets of modern living. The energy balance of the various countries of the world shows the increasing importance of atomic energy in providing electric power. The time is fast approaching when thermonuclear power plants will become routine aspects of our technology. Various categories of nuclear reactors--in research, in transportation, in energy--are sources of gamma-neutron emission which impinges on the attending personnel during a routine workday.

Considerable attention has been given to safety measures from the very inception of nuclear energy technology. It is generally recognized that this is one of the safest fields of endeavor. Yet, despite their rarity, radiation-related accidents do occur in various countries; they affect largely research reactors and the so-called critical assembly sites. Human irradiation may be significant in such cases and may have an adverse effect on health. In addition, we cannot neglect the possible military use of nuclear energy intended to injure people with gamma-neutron radiation from nuclear explosions.

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Gamma-neutron are released by isotope sources and accelerators of charged particles. Finally, the passengers and crews of high-flying future jets will encounter weak gamma-neutron radiation which presently affects only the cosmonauts.

In order to evaluate the levels of radiation to which humans are subjected and the possible health consequences that this may have, it is necessary to determine the distribution of the radiation dose on the human body.

The manual "Tissue Doses of Neutrons in the Human Body" [32] contains data on dose loads imparted to a human phantom by monoenergetic monodirected neutrons. The information given makes it possible to calculate body distribution of a dose load from a neutron irradiation of an arbitrary spectral-angular distribution.

However, there are virtually no pure neutron radiation sources. Neutron emissions are accompanied by gamma rays, a fact which seriously alters the conditions under which humans are irradiated. Radiation weakens in the body and its interaction with biological tissue is a very complex factor dependent on the energy and the angular distribution of radiation. Consequently, there was a need for information on deep dosages of monoenergetic monodirected photon emission in the same model of the human body as used in the neutron manual [32]. Such information, obtained by the authors, is presented in this book.

A step-wise approach was used to determine dose distribution in the body. Initial consideration is given to the formation of the gamma-neutron emission field which acts on humans. Subsequently, computers were employed to calculate the body dose load. The latter undertaking utilized extensively the data in the manual in question [32].

In addition, use was made of anatomic data on the location in the human body of certain critical organs and, in conjunction with computer techniques, the dose distribution among these organs was calculated. Criteria are presented for the radiation effects on the body which take into consideration doses at critical organs.

Calculations were taken under the various conditions under which humans are irradiated. This made it possible to evaluate the influence of various factors on dose loads, such as the spectra and composition of radiation, the selected coefficient of neutron quality, distance from the source and the dimensions of the room, and the orientation of the human subject in the radiation field. The results are analyzed.

The material in the book is largely original. It is intended for those interested in radiation safety, dosimetry, and biomedical problems related to the use or effects of gamma-neutron radiation. However, localized irradiation is not discussed.

This is the fourth in a series of books on external radiation dosage being planned by collaborators of the Institute of Biophysics of the Ministry of Health USSR. In addition, Atomizdat has already published the manual alluded to here, i.e., "Tissue Doses of Neutrons in the Human Body," which was prepared jointly with the workers at the Physical Energy Institute in Obninsk, and a book by I. A. Bochvar et al. entitled "Methods of IKS [expansion unknown] Dosimetry." A book by V. I. Popova, "Methods of LPE [expansion unknown] Spectrometry of Ionizing Radiation," is due to be published.

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The authors are indebted to I. K. Kalugina, G. V. Noskova, O. V. Cherkashina, O. N. Chernova, and T. K. Shmeleva for their assistance in the preparation of this book, and to S. N. Kraytor and I. V. Filyushkin for useful discussions on the formation of emission fields in closed space.

The authors will welcome comments from interested readers.

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PHYSIOLOGY

THE QUESTION CONCERNING THE ELECTROSTATIC FIELD OF HUMAN BEINGS

Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 6, No 1, Jan-Feb 80 pp 148 152

[Article by Yu.V. Tornuyev, Novosibirsk Institute of Physiology]

[Text] The presence of measurable electric fields near living organisms has by now been reliably established (1-7). These fields originate from diverse sources and they provide information on the functional condition of the organism.

The fields of relatively high frequency that are associated with the activity of the human heart muscle have been most fully investigated. Methods have been developed for differentiating fields originating from different sources and the informative significance of these fields has been evaluated (3-7).

So far, however, the problem concerning the measurement of an organism's infra-low-frequency fields and the mechanisms of the field's genesis have practically been bypassed by the researchers.

The great interest that has of late been exhibited toward contactless methods of extracting information on the electrophysiological processes in an organism puts on the agenda the question concerning the mechanisms of formation and the informative significance of electric fields of the low-frequency range.

The first experiments involving the recording of low-frequency electric fields (from 0.1 to 10 c/s) in the air were carried out by us by means of synchronous accumulation (1). Analysis of the results of these experiments testifies to the presence near human beings and animals of low-frequency electric fields, the amplitude of which declines as the frequency increases. However, the method used in the experiment did not allow us to obtain the information in a form accepted in electrophysiology and it did not unequivocally answer the question concerning the mechanisms underlying the field's formation.

In the studies (3,4), man's electrostatic field in the air is examined and its direct dependence on the organism's functional state is demonstrated. However, with the sensory elements used by the author, it was not possible to study the field's fine structure; these experiments did not provide for continuous recording of the field's potential over extended time spans.

It was the aim of the present study further to investigate the basic characteris-

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tics of the electrostatic and infralow-frequency fields formed by a living organism as well as the mechanisms of the field's formation.

Methods

For measuring the electric field, we proposed the method of recording the current carried by the conductor (pickup) moving in the field investigated (5). As pickups, we used metal balls or disks 10 mm in diameter that were embedded on a non-conducting bar and that oscillated with a frequency of approximately 1 c/s. The input stages of the measuring amplifier were effected on the basis of domestically produced MDS transistors and they maintained a zero drift of 160-200 microvolt for 3 hours. By means of a pen recorder, we recorded the envelope of the alternating current that was carried in the pickup during its movement in the field investigated.

Measurement of the intensity or potential of the electric field of man relative to the ground was carried out in an insulated chamber measuring 2.5 x 2.5 x 2.5 m with an attenuation factor of 50 c/s over 100. The test subject was placed in a horizontal position approximately in the center of the chamber, in order to reduce any field recording deviations resulting from the study subject's dissymmetry relative to the chamber's walls (6-9). Aside from the test subject and the field pickups, the chamber did not contain any measuring instruments or extraneous objects. In order to eliminate the undesirable influence of a triboelectrical charge on the results of the experiment, the test subjects were divested--either partially or completely--of their clothes, which are capable of building up an electrical charge and sustaining it for an extended period.

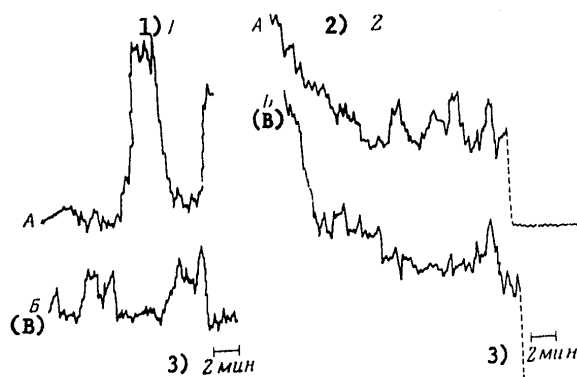
The grounding of the test subject was carried out at least 5 minutes before the beginning of the recording; the grounding electrode was placed at the lower third of the test subject's right shin. The calibration of the measuring circuit was done by the method set forth in the studies (6,7) in the field of a parallel-plate capacitor.

Presentation and Discussion of the Study Results

The results of the experiments conducted demonstrate that in the immediate proximity (5-10 cm) of the human body there exists a measurable electric field that is made up of several components--a stable component and variable ones. The potential difference of the electrostatic field relative to the ground at a distance of 5 cm from the surface of the test subject's body reaches 1,000 millivolt; in the first 10-20 minutes of the experiment, the level of the electric field is reduced, but subsequently the average magnitude of the signal recorded stabilizes. In this case, we observed--against the background of a relatively slow drift--quasiperiodic field potential oscillations ranging from 2-5 per minute to 1 per 2 minutes; besides, the slower constituents of the signal had a relatively large amplitude. Figure 1 shows characteristic traces of the electric field of two test subjects, which were recorded 2 and 10 minutes after the beginning of the experiment at a distance of 5 cm. In both cases, the quasiperiodic oscillations are clearly traced; and as illustrated in Figure 2, the electrograms do not show any substantial difference in regard to the amplitudes and the general tendency of the signals recorded--regardless of whether or not the test subjects were grounded. Figure 3 presents

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Figure 1. Typical Electrograms of a Human Field for Different Test Subjects
(Distance to the Field Pickup: 5 cm)



Key:

1. 1: (22 June 1976) Quality traces of electric field changes for two test subjects, T. (A) and V. (B)
2. 2: (26 June 1975) Electric field traces for two test subjects, O. (A) and T. (B). On the left side of the trace--the process of charge dissipation; on the right side--the background noise in the chamber with the test subject absent immediately after the termination of the experiment.
3. 2 minutes

the electrograms of a human field (A), the changes in the (background) noise level in the insulated chamber with the test subject being absent (B), the field changes occurring with placement of the pickup in a standard electrostatic field (C) and in an infralow-frequency field (D) of a parallel-plate capacitor. Comparing the traces, one ascertains that the signals recorded must be related to the test subject's presence in the chamber.

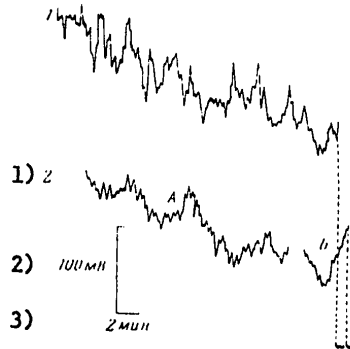
Figure 4 shows the comparative traces of a human field and of a field recorded in the proximity of an electrified object. Evidently, the two traces show an identical tendency. The change in the potential of the field near the electrified object occurs in an exponential fashion in conformance with (10) and the potential recorded tends toward the background noise value; there are no oscillations. Through inclusion of a measuring amplifier 15-20 minutes and more after the beginning of the experiment, it was possible to record noises (with the test subject being absent from the chamber) or signals resembling those presented in Figure 1,1. This circumstance allowed the conclusion that the signals recorded--in particular the first sections of the field trace--are not a result of the transient processes in the circuits of the capacitor or of the filters.

In all probability, the electric fields recorded by us can be attributed also to that class of fields of bio-objects that are explained by the existence of an electrical surface charge or of a steady distribution of charges on the test subject's body surface (7). The surface density of such a charge can reach magnitudes

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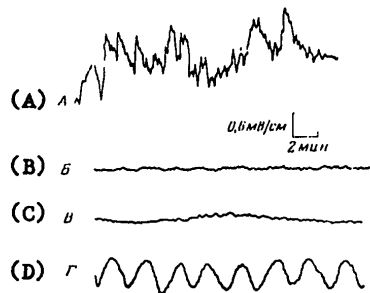
Figure 2. Electrograms of a Human Electric Field Obtained on Different Days
(1: 23 June 1975; 2: 20 June 1975)



Key:

- 1. A: Subject not grounded; B: Subject grounded
- 2. 100 millivolt
- 3. 2 minutes

Figure 3. Electrogram Models



Key:

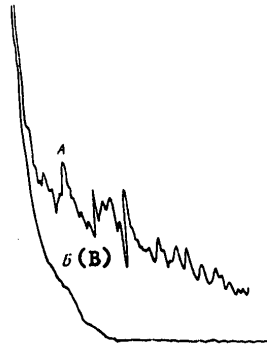
- A. Typical trace of a field near a person
- B. Time-dependent zero drift with the test subject absent from the chamber
- C, D. Change in the signal level upon exposure of the pickup in a standard electrostatic field and in an infralow-frequency field

ranging from 10^{-5} to 10^{-8} coulomb/cm² (8) and the formation, buildup and diffusion of this charge on the body surface occurs in the process of lively activity on the part of the individual (8). When the individual changes from an active to a passive state--which coincides with the beginning of the experiment--one observes a process of dissipation or neutralization of the charge and, as a result of this, a reduction in the intensity of the field. In comparing the processes of dissipation of the charges recorded near the person and near the electrified object (with the rates of humidity of the surrounding air being equal), one perceives a difference between them. The duration of dissipation from the electrified object depended on the intensity of the charge and on the properties of the insulator (10), and in the course of the experiment we never observed any increase in the field's potential.

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Figure 4. Comparative Electric Field Traces Recorded Near a Person (A) and Near an Electrified Object (B). Distance to the Field Pickup: 5 cm



As regards the measurement of the electric field near the person, the process of dissipation of the charge conformed only at the beginning of the experiment to the patterns shown in study (10). The electric field never reached the zero level; we observed oscillations of the signal level and in a number of instances a drift to the side of augmentation. Nudity of the test subject, grounding of the test subject, a high degree of humidity of the surrounding air--all of these helped considerably in removing the electrical charge from the body surface. However, there is every reason to assume (2,7) that during the time coincident with the beginning of the experiment the dynamics of the electric field near the person are for the most part determined by the electrical charge and the formation of that charge is closely related to active motion on the part of the person. This appears to be corroborated by the results of experiments involving recording of the mechanical manifestations of the activity of the heart (2,7), the results of a theoretical investigation of the process of dissipation of the electrical charge, and the results of contact measurements of the field potential of the human body that were carried out by us in study (10).

The fact that after the dissipation of the electrical charge from the surface of the grounded human body the electric field does not reach the zero level--as follows from study (10)--may be indicative of some kind of balance between the processes of charge dissipation and charge sustainment, and the infralow-frequency oscillations of the field level upon removal of the triboelectrical charge may be an indication of the dynamics of this process.

The studies (3,8,9) put forward hypotheses concerning the formation of a human electric field of a nontriboelectrical nature; they show this field to be related to the functional state of the organism (3,4); in this case, however, no allowance is made for the phenomena occurring at the interface of the two media (11,12) (concretely, between the human body and the air) or for the contact phenomena occurring upon application of the ground electrode during the dissipation of the electrical charge, which phenomena may lead to the emergence of a measurable

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electric field. The results of the contact experiments--conducted by us in study (10)--appear to corroborate the hypothesis advanced. At the same time, it is doubtful whether one can assume that in the experiments (3,4) the triboelectrical charge was totally removed from the body surface; one cannot rule out the possibility that the process of sustaining that charge is associated with friction of the body against the air during respiration, during the passage of a pulse wave along the body. The infralow-frequency oscillations of the field potential may be a result of changes in the electrical resistance of the body's integuments and vessels.

Thus, what is required is a more exact approach to the solution of the problem concerning the mechanism of the electrostatic field formation by the human organism as well as greater accuracy in the removal of the triboelectrical charge.

Conclusions

1. Near the human body, an electrostatic field has been recorded.
2. The presence of infralow-frequency oscillations of the level of man's electrostatic field has been established.
3. In interpreting the results of contactless measurements of electrophysiological processes, one must take into consideration the presence of high-amplitude oscillations of the field potential that in all probability are not directly related to these processes.

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CORRELATION INDICATORS OF BRAIN ELECTROENCEPHALOGRAMS DURING EMOTIONAL STRESS

Baku KORRELYATSIONNYE POKAZATELI ELEKTROENTSEFALOGRAMM GOLDVNOGO MOZGA PRI EMOTSIONAL'NOM STRESSE in Russian 1979 signed to press 18 Jan 80 pp 2-7, 129

[Annotation, preface, introduction and table of contents from book "Correlation Indicators of Brain Electroencephalograms During Emotional Stress", by A.A. Mamedov, A.I. Karayeva Institute of Physiology, Azerbaijan SSR Academy of Sciences, Izdatel'stvo "Elm", 1200 copies, 129 pages]

[Text] The book covers one of the urgent problems of modern neurophysiology and practical medicine, the study of the central mechanism for emotional stresses. The systems approach is used to analyze the results obtained from correlation analysis of EEG-potentials of the brain on automated systems, including computers. The outlook is shown for the use of these systems.

The book is designed for a broad group of specialists who are working at the junction of neurophysiology, medicine, mathematics and electronics, and in the field of biological and medical cybernetics.

It is printed by decree of the editorial-publishing council of the Azerbaijan SSR Academy of Sciences.

Editors: K. V. Sudakov, G. G. Gasanov, A. I. Shumilina

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Preface	

This book is dedicated to the bright memory of my teacher, Lenin Prize laureate, Academician P. K. Anokhin.

A study of the central mechanisms for stress, which is acquiring an emotional aspect to an ever greater degree, is among the most urgent problems of modern neurophysiology and medicine. Rapid scientific and technical progress, having created complicated conditions of adaptive behavior, requires the processing of an enormous flow of diverse information on human biological functions and social activity.

The WHO experts indicate that emotional stresses caused by an increase in the tempo of life, urbanization, information overload and adynamia, in 70% of the cases result in different vascular affections of the brain, heart (hypertonia, myocardial infarct, insult, atherosclerosis, etc.). They also lead to the development of neurotic conditions, mental disorders and disorders in normal human adaptation to social conditions of life.

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The Soviet neurophysiologists, based on the teaching of I. P. Pavlov on nervosism, have established the paramount reason for diseases as primary disorders in the cerebral functions as a result of frequently repeating emotional stresses. Without belittling at all the most fully developed endocrine-biochemical aspect of stress of G. Sel'ye, it should be stated that they are most often secondary reactions of a pathological process that has primarily been formed in the central nervous system. In recent years therefore, questions referring directly to nerve mechanisms have occupied the central place in the problem of emotional stress. Special scientific sessions, and all-union and international conferences have covered this aspect of emotional stress and its role in cardiovascular pathology, and in different cerebral-visceral disorders.

The monograph of Doctor of biological sciences A. M. Mamedov also treats this question.

The author is a student and follower of Academician P. K. Anokhin, the founder of the theory of the functional system. Many years of work in P. K. Anokhin's laboratory determined the main feature of this monograph, namely, the broad use of the theory of the functional system in analyzing mechanisms for cerebral organization of different stages of emotional stress. An engineering education in combination with the lofty erudition of the neurophysiologist permitted A. M. Mamedov to make a special mathematical analysis on computers of the known phenomenon. This is the phenomenon of the appearance of a regular, ordered rhythm of electrical activity (stress rhythm) of 4-7 oscillations per second that develops in different cerebral structures under conditions of stress factors.

By analyzing the conditions for formation of emotionally negative stimulations, and their transition to a static state, the author gives very great significance not only to physical factors, but quite correctly also to purely informational characteristics of the "conflict" situations. Here the long-maintained "signalless" situation with low probability of "foreseeing" the emotionally unpleasant stimuli is the most dangerous for the organism. These stimuli result in an irreversible process, and in the formation of a new cerebral condition that differs from the normal and is characterized by disrupted spatial-temporal interrelationships between the cortex and the subcortical structures.

These finest cross-correlation shifts are based on changes in the polarization of the analyzed structures due to shifts in the neurochemical mechanisms. Since such a condition of the brain is characterized by a number of somatic-autonomic disorders, it can be called the "cerebral-visceral syndrome" of emotional stress. It is one of the initial pathogenetic factors for the formation of pathological shifts in different functional systems of the body, including the cardiovascular system.

A careful correlation analysis on the computer of the stress rhythm in different cerebral structures permitted A. M. Mamedov to find the characteristic dynamics for emotional stress, and the features of the interrelationships between the cortical-subcortical formations at different stages of its development. In our opinion, the most important phenomenon in this respect is the detection of laws governing the change in phase shifts and functional links between the electrical potentials of the hypothalamic structures, the cortex of the large hemispheres and the reticular formation when experimental emotional stress is formed. Of especial interest in this respect is the establishment of the fact that at the later stages of

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emotional stress, the functional links between the hypothalamic formations and the cerebral cortex are diminished, and on the contrary, are intensified with the reticular formation of the brain. These neurophysiological data shed light on the problem of the so-called "defense inhibition" that was formulated by Academician I. P. Pavlov.

Based on the new, original data that A. M. Mamedov obtained, one can consider that a reduction in the functional links between the hypothalamus and the cortex, and a number of structures in the cerebral limbic formations is the basis for the "defense inhibition" of cortical components during emotional stresses. On the other hand, these same mechanisms can be the basis for the development of neurotic conditions that are often a consequence of strong emotional over stresses.

The book of A. M. Mamedov is an important stage in the study of emotional stress. It makes a significant contribution to the investigation of the central mechanism for emotional stress. It goes without saying that it is of considerable importance for specialists of varying profile who are interested in this problem.

Corresponding Member of the USSR Academy of Medical Sciences, Professor K. V. Sudakov

Introduction

According to the biological theory of emotions of Academician P. K. Anokhin [5,6], emotional excitation has been included during evolution at that point of the central architecture of the functional system where feedback is used to compare the parameters for the result of a purposeful behavioral act with the parameters that were previously prepared in the acceptor of action results. This is based on afferent synthesis of diverse external and internal factors. An important role among these factors belongs to the motivational stimulation that dominates at the given moment.

When the parameters from a completed action coincide, the developing need is satisfied. This is accompanied by positive emotions. On the contrary, when these parameters do not coincide, negative emotions develop. When there is a prolonged discrepancy in conflict situations, they increase and are intensified.

A characteristic feature of negative emotional stimulations is their capacity to be retained for a long time in the CNS even after the stimuli have stopped. This is precisely the feature that leads to stabilization of stimulations and is the most dangerous for the body.

Expanded pathological bonds that are formed on this basis between the environmental factors and are mediated through the effect of the cortex of the large hemispheres are a mandatory physiological condition for the transition of emotions to the stationary form, on a high level of excitability of the emotiogenic subcortical cerebral formations.

The most important questions in emotional stresses are those that are associated with the spatial-temporal features of cortical-subcortical interrelationships of the brain when emotional stress is formed and their correlation with the autonomic components, the presence and the role of pacemakers for emotionally negative reactions, as well as the conditions that promote the transition of negative emotional stimuli to the static condition. A study of this basic problem is unthinkable without the appropriate mathematical analysis and modern electronic equipment, including computers.

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Taking into account the random nature of the electrical oscillations in the brain, and their probability-statistical organization, the use of statistical parameters of EEG-potentials that develop during negative emotional states as the indicators for the emotional reaction becomes very effective. The application of statistical methods, and in particular, of correlation analysis, with all the randomness of complicated EEG-oscillations, permits isolation of individual, stable parameters that objectively and accurately characterize the specific features of interrelationships in the studied process.

In reflecting on the means for further development of electroencephalography, Academician M. H. Livanov [72] was convinced that "it is precisely a study of the interrelationships of the variously localized processes in time that is promising for a clarification of the main laws governing the mechanisms for cerebral activity. In fact, localization of even the simplest cortical functions is not a single point. It is always complicated and dynamic, reflecting the interrelationships of numerous cortical and subcortical systems." In this respect it is precisely correlation analysis that is one of the effective methods for studying spatial-temporal interrelationships between the cerebral structures. The establishment [72,73] of the physiological significance of the cross correlation coefficient permitted a number of important conclusions on the conditions for transmitting a stimulus between the cortical analyzer systems. The important role of coherence, dispersion and phase shifts of EEG-oscillations in this transmission was shown later, in addition to the functional bond.

A study of the central mechanism for emotional stress from the positions of systems analysis, and on the basis of mathematical methods characterizes the systems-cybernetic approach to the research object. In this respect, it is shown in the second section of the book that when physiological information is processed on the computer, the application of automated systems becomes very important. This especially refers to those where the computer is used not only as a "calculator," but as the actual controller of the experiment, becoming its organic participant [72]. This type of system is the prerequisite for the future creation of a unified, optimally conjugated brain-computer system that promotes the effective solution of problems of controlling complicated objects.

Thus, the development and final success of modern neurophysiological research are determined to a considerable measure by the union of traditional physiology with the ideas and methods of precise sciences.

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STUDY OF DIFFERENTIAL SENSITIVITY TO CHANGES IN DURATION OF TONAL SOUNDS

Leningrad FIZIOLOGICHESKIY ZHURNAL SSSR IMENI I.M. SECHENOVA in Russian
Vol 61, No 6, 1975 pp 938-944

[Article by V. I. Medvedev, N. D. Bagrova and A. A. Sagal, Military
Medical Academy imeni S. M. Kirov, Leningrad, submitted 5 May 74]

[Text] Studies were made of differential sensitivity of man to duration of tonal stimuli in the range of 50-700 ms. The threshold method of constant differences between stimuli (AX method) and combination of the method of multiplication of duration by two or three with the AX method (AB methods) were used. Differential threshold were obtained as linear functions of standard duration, the limen being significantly higher with method AB than with AX. The threshold levels were related to multiplication factor, type of psychometric functions and individual differences between subjects, but they were unrelated to conditioning time.

Differential sensitivity is one of the most important indicators of activity of the human analyzer system, of quantitative characteristics of the latter's capacity to reflect local changes in time and space features of man's habitat [1]. Numerous works of psychophysicists have dealt with this capacity, and they constituted the main quantitative description of functions of analyzer systems as a whole [4, 6, 13, 16]. Direct quantitative evaluation of the capacity to reflect time-related characteristics of signals in the form of determination of time-related sensitivity and capacity to differentiate between duration of stimuli are of special significance. Expressly this aspect of analyzer function has been studied much less comprehensively [8, 12, 14, 15]. Data have been obtained by qualitatively different methods, without comparison to data referable to other modalities. The main cause of discrepancy between the obtained data is inadequate testing of optimality of psychophysical methods used [8, 14, 15]. Thus, some authors did not adhere to any standard techniques (for example [8, 10, 15], while in other works there is no clearcut description at all of the

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psychophysical procedures used [3, 7, 8, 14, 152. Control of the method is particularly important in view of the considerable values of time-related error, which could be expected when studying time sensitivity [17, 18].

This circumstance imposes certain requirements on the search for the optimum psychophysical method that would minimize and stabilize the time-related error. We have established [2] that the optimum in this respect is a combination of the supraliminal method of multiplication with the threshold method of constant differences between stimuli (abbreviated constant method). This combination decreases by several times the time-related error, as compared to other combinations (set and separation, constant and separation, set and multiplication), even in the absence of alternation of pair elements: standard -- comparison tone within the range of the fixed order of stimuli. This makes it possible to undertake a systematic study of sense of time in relation to duration of tonal sounds in the range of 50-700 ms.

Methods

We used two methods to evaluate differential sensitivity. The first was the liminal method of constant stimulus differences in its nonsymmetrical modification [1]. In this modification, there is a dissimilar number of stimuli x_i ($i = 1, 2, \dots, n$) among the comparison signals, which are lesser or greater than standard signal A, for which the differential threshold (DT) is calculated. In this study, we used only one x_1 signal that was shorter than the standard (Figure 1). Accordingly, the experimental results enabled us to plot only one psychometric function, the ascending ogive corresponding to evaluation of the signal by means of the judgment category of "this signal is longer than the standard." This method permits rapid gathering of data and evaluation of differential sensitivity (DS) without appreciable decrease in accuracy of evaluation, as compared to the classical symmetrical method [1, 9]. In the following, we refer to this method as the direct method of evaluating DS or the AX method [9, 10].

The second was the supraliminal multiplication method combined with the triple symmetrical method of constant stimulus differences, which was described in detail previously [2]. Let us recall that, in this method, for each tone of standard duration A we selected comparison tones x_i distributed in relation to B as mathematical expectation, B being two or three times greater than standard A: $B = kA$, $k = 2$ or 3 . In the following, we refer to these as indirect methods AB-2 or AB-3, with k equaling 2 or 3, respectively. It is logical to refer to AB as indirect methods, because evaluation of DS is an ancillary procedure, in addition to their main purpose, that of assessing the capacity to scale sounds.

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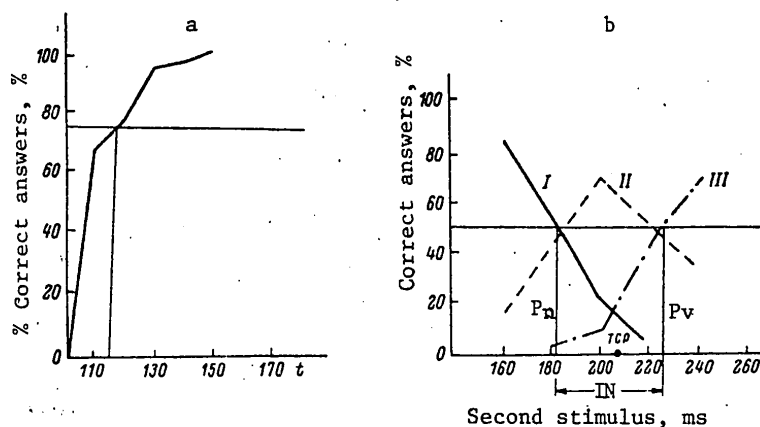


Figure 1. Psychometric function with nonsymmetrical method of constant stimulus differences (a) and triple category method of constant stimulus differences (b)

I) for y_1 II) for y_3 III) for y_2

[Pn, Pv and IN explained in the text]

With methods AX and AB, the tones were presented to subjects in pairs: first standard A then comparison tone x_i ($i = 1, 2, \dots, n$). With the AB methods, the tones were evaluated in three judgment categories y_j ($j = 1, 2, 3$). Thus, with method AB-2, these categories sounded as follows: y_1 --"the second signal is less than double the length of the first one; y_2 --"... it is exactly twice as long as the first" and y_3 --"... it is more than double the first one." Accordingly, with method AB-3 we determined the distribution of comparison signals in relation to the category of "three times longer signal." For this reason, we obtained three psychometric functions with the AB methods (Figure 1b).

All of the sounds had a frequency of 1000 Hz and volume of 70 dB above the audibility threshold. The time thresholds were determined for standard durations: $A = 100, 200, 300, 500$ and 700 ms with method AX, and $A = 50, 100, 200, 300$ and 500 ms with AB methods. For each standard A we selected on the linear second scale $n = 5-7$ gradations for duration of comparison tones x_i with scale graduation of $\delta = 10-30$ ms, i.e., so that the interval between the shortest and longest comparison tones would be small as compared to the standard, $n\delta < A$.

A ZG-10 sound generator served as the source of the sounds. A mechanical time relay designed by V. P. Morozov [3] was used as a timer; the

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error factor constituted 3-5 ms. The tones were delivered monaurally through TD-6 calibrated dynamic telephones.

Subjects (students) ranging in age from 22 to 26 years participated in the experiments. There were 10 subjects used in each series, and 6 participated constantly in all tests.

The experiments were conducted in a soundproof chamber. The subjects listened to a pair of signals and entered their estimates on a special form. The pairs of signals were delivered at intervals of 5 s without warning signals. The comparison sounds were delivered with equal probability and independently of one another. The test lasted 10-15 min.

In each experiment, each time gradation was presented 10 times, i.e., the test consisted of presentation of 70 pairs of sounds. There were 6 experiments with each standard duration, which constituted 2520 measurements for a group of 6 subjects with each group determination of the threshold.

Each sequence of tests with a fixed group of subjects and fixed method and standard was combined into a series of tests. In all, there were five series by each method.

In method AX, we took the segment on the time scale equal to the distance between the point of standard stimulus A and projection of ogive point at the accuracy level of 75% as the magnitude of differential threshold L_u (Figure 1a). In view of the high accuracy of the method, when plotting the ogive we limited ourselves to graphic interpolation.

In the AB methods, the psychometric functions for ogives were plotted by the least squares method using the Muller-Urban scale. The threshold according to Urban L_u was calculated as half the uncertainty interval, i.e., half the distance between mathematical expectation $P_v = M(x/y_3)$ for the ascending ogive and $P_n = M(x/y_1)$ for the descending ogive: $L_u = P_v - P_n/2$. For the frequency distribution $P(x/y_2)$ we calculated the threshold according to Fechner L_f as the standard deviation of distribution: $L_f = \delta x/y_2$ (Figure 1b).

The laborious procedure of calculating the thresholds was performed on a Dnepr computer. We used one-factor regression analysis [5] to determine the values as functions of the experimental factors tested. The reliability of group measurements was tested using the criterion of Student (Ibid).

Results

Temporal differential thresholds as a function of duration of sounds: Figure 2 illustrates the initial experimental results:

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psychometric functions obtained by the AX method for different standard times and averaged for each standard and 6 subjects, and for all 6 experimental days. We see that they are similar to one another on the scale illustrated, when increment of variable stimulus ΔX is plotted on the x-axis, as percentage of standard A, i.e., $\Delta x/A\%$ ($\Delta X = X-A$). Analogous similarity of families of psychometric functions was present with the other methods. This means that $L/A \approx \text{Const.}$, and hence there are two assumptions: 1) correlation (close to linear) between absolute DT and value of standard A, i.e., hypothesis $L(A) = aA + b$; 2) close to constant ratio of DT to A, i.e., hypothesis $W(A) = LA/A \approx \text{Const.}$ The main procedure of processing the results was concerned with comprehensive examination of these interrelated hypotheses.

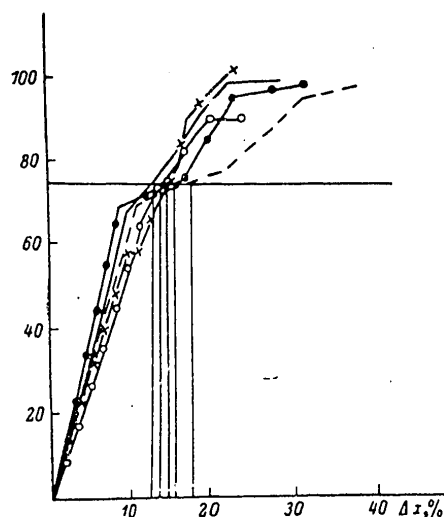


Figure 2.

Family of group psychometric functions for various standards with the AX method. Explained in the text.

other, in the same manner from theogives, we can detect an appreciable difference: the mean difference $L_u = L_u, AB - L_u, AX = 12.2 \pm 1.0$ ($\gamma = 12.2$, $p < 0.001$), i.e., L_u is considerably greater for the AB methods than AX.

At the same time, within each of the above classes, we observe a distinct correlation between location of the curves and factor of sound multiplication with the AB methods, i.e.: the curves for data with sound tripling AB-3 method) are above the corresponding curves for data with doubled

Threshold (absolute) as a function of standard sound A. As can be seen from Figures 3 and 4, the thresholds increased monotonically with increase in standard duration. Thus, with increase in the standard from 100 to 500 ms we observed an increase in DT: from 18 to 68 ms with the AX method and from 23.2-33.2 to 73.2-137.9 ms for the AB method. With all the differences between them, the set of ascending curves $L(A)$ can be divided into two classes: flatter (slowly ascending) and steeper curves. The former include thresholds L_u (i.e., those calculated according to Urban from cumulative ogives) using AX and AB methods, and the latter refer to L_f (thresholds determined according to Fechner from frequency distributions) with the AB methods.

If we compare the values of DT obtained by the AX method, on the one hand, and AB method, on the

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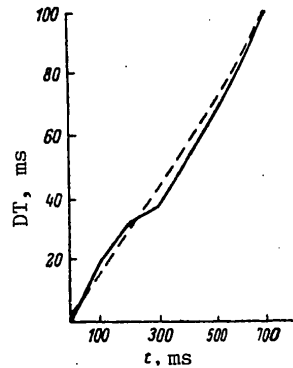


Figure 3.
Differential thresholds as a function of duration of sound with method AX. Dash lines refer to results of analysis of one-factor regression correlation between these levels.

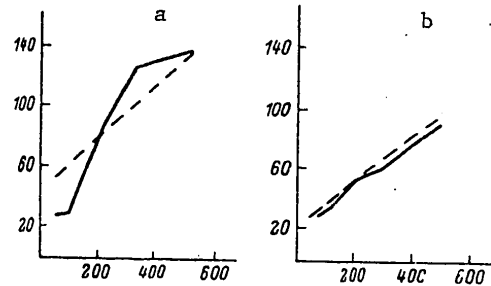


Figure 4.
Values of differential thresholds as a function of duration of sound with method AB
Top--AB-2; bottom--AB-3
a) for frequency distributions
b) for ogives

duration of sounds (AB-2 method). The mean difference between values of DT obtained under conditions differing in this way constituted 12.75 ± 5.3 ms as a whole ($p < 0.05$). It was quite significant for L_U ($\Delta L_U = 10.8 \pm 0.8$, $\gamma = 13$, $p < 0.01$), and insignificant for L_F ($\Delta L_F = 14.7 \pm 9.4$ ms) in view of the sharp increase in difference with $A = 500$ ms (the difference was more uniform and therefore significant for the three lower standards).

Finally, $L_F > L_U$ for each AB method: $\Delta L_{F-U} = 21.34 \pm 11.8$ ($\gamma = 1.82$, $p < 0.05$) for AB-2, $\Delta L_{F-U} = 31.2 \pm 13.8$ ($\gamma = 2.26$, $p < 0.05$) for AB-3 and for both AB methods as a whole, $\Delta L_{F-U} = 26.35 \pm 8.68$ ($\gamma = 3.04$, $p < 0.01$). It must be emphasized that the low value of $L_F - L_U > 0$ with each method individually is related to the drastic increase in always positive difference ΔL_{F-U} with increase in the standard.

The obtained differences, not only for different values of DT but for curves $L(A)$ as a whole, were checked by the method of regression analysis (using a Dnepr computer) within the framework of verification of the hypothesis of linear correlation between DT and duration of sound t : $L(t) = at + b$ [according to data from interpolation of function $L(A)$]. The results of one-factor analysis summarized in the Table in the form of values of parameters a and b of this equation for different tested conditions demonstrated good agreement of the experimental data with the above-mentioned statements that curves $L(A)$ are correlated with

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the factors determining them (method, frequency, distribution, from which the DT were obtained).

Values of parameters of linear regression correlation between differential thresholds and duration of sounds

Method	L (t)		W (t)	
	a	b	a	b
AX	0.14	1.02	-0.00005	0.164
AB-2 {	0.25	0.5	-0.00014	0.207
	0.119	12.2	-0.00014	0.213
AB-3 {	0.16	46.35	-0.0002	0.412
	0.123	22.8	-0.00022	0.289

Relative threshold as a function of value of standard: The logical consequence of linearity of function $L(t)$ is the approximate constancy of Weber's function $W(t) = L(t)/t$. A more detailed study was made of relative value of thresholded $W(t)$ as a function of t by means of verification of the hypothesis of linearity of functions $W(t)$ in the function of sound duration using regression analysis methods. As can be seen in Figures 5 and 6, function W for methods AB-2 and X was a line that was virtually parallel to the x-axis. A negligible decline of $W(t)$ with increase in t was inherent in the AB-3 method.

At the same time, we demonstrated relatively high values of $W(A)$ with the lowest standard, $A = 50$ ms for the AB methods. Thus, for AB-2, $W(50)$ constituted 0.35-0.45 and for AB-3 $W(50) = 0.55-0.61$. The mean for all standards \bar{W} constituted 0.12-0.18. The mean difference W was significant for the standard $A = 50$ ms and even for another separate $A = 50$ ms standard. Thus, for AB-3 increasing the standard from 50 to 500 ms caused $W(A)$ to decline from 0.55 to 0.172.

These figures conform well with the data of most other researchers [12, 15]. However, they are higher than the ones obtained in [14], where only descending series of the considerably less precise (nonoptimum) method of boundaries was used.

The other factors (method of examination, factor of multiplication, type of distribution) had an analogous effect on $W(A)$ as they had on $L(A)$.

DT as a function of conditioning time: Systematic comparisons of DT demonstrated on successive experimental days by different subjects failed to reveal any consistent changes in the values as a function of conditioning time ($p > 0.05$). Maximum deviation of DT of some subjects

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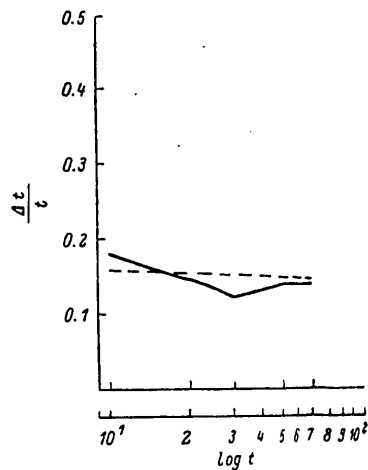


Figure 5.

Correlation between Weber's function $W = \Delta t/t$ and duration of sound with the AX method. Dash line shows $W(t)$ as a linear regression function of t .

of time discrimination. Thus, in the double method of constant stimulus differences the threshold constituted 15-21% of the standard, and with tripled sound the differentiation threshold reached 17.2-42% of the standard.

from the mean values thereof did not exceed 15-20% of the standard deviations of arithmetic mean DT (see also the preceding article for a more detailed description of relevant facts).

Conclusions

1. The auditory analyzer of man identifies the duration of sound of the order of fractions of seconds rather accurately. The thresholds of discrimination of duration of a standard sound in the range of 100-700 ms constituted 12-18% of the standard and conformed with the psychophysical law of Weber-Fechner.
2. The differential time thresholds can be obtained by multiple methods of standard stimulus differences. With increase in multiplicity there is an increase in threshold

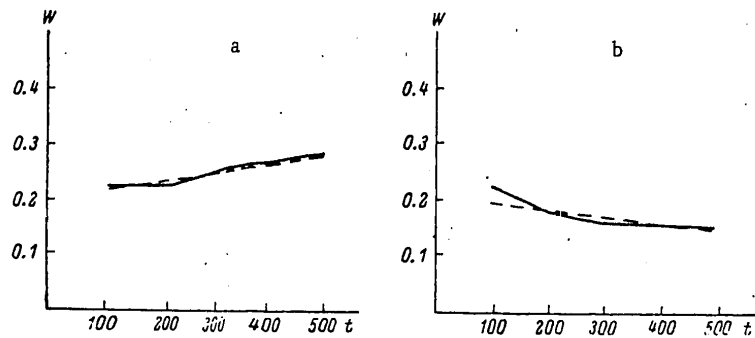


Figure 6. Correlation between Weber's function $W = \Delta t/t$ and duration of sound for the AB method. Top--for AB-2; bottom--for AB-3; a--for frequency distributions; b--for ogives.

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3. The highest threshold of discrimination was demonstrated in our testing of perception of short signals (50 ms). With multiplication by 2, the threshold constituted 35-45% of the standard and by three, 55-61%.
4. The levels of differential thresholds rose linearly with increase in curation of standard sounds and they depended appreciably on the psychophysical method of testing and the process for determining the threshold.
5. We demonstrated appreciable individual fluctuations of sensitivity. At the same time, we failed to demonstrate an effect from conditioning (systematic variation of thresholds on successive test days).

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EFFECT OF DIFFERENT WORK-REST SCHEDULES FOLLOWING 64-72 HOURS OF WAKEFULNESS

Moscow FIZIOLOGIYA CHELOVEKA in Russian No 4, 1980 pp 686-694

[Article by A. N. Litsov]

[Text] It follows from published data (1-7) that the success with which man adapts to an altered schedule of daily activity goes a long way in determining his capability for returning to and maintaining qualitatively and quantitatively wholesome sleep. It has been revealed in this case that the dynamics of sleep may be interpreted not only as an indicator defining (in integration with others) the degree to which the individual retunes himself for a new daily schedule, but also as a means for maintaining his working efficiency at the needed level. Unfortunately the literature on the psychophysiology of sleep still lacks sufficiently persuasive data necessary both for development of daily cyclograms of operator activity and for organization of measures to keep the working efficiency of operators optimum in the "sleep-wakefulness" cycle. The materials presented in this communication, which reveals the psychophysiological features of the sleep of an individual following different schedules of daily activity in a confined space, and after prolonged continuous wakefulness (64 and 72 hours), may have certain theoretical and applied interest in this respect.

Methods

The research was conducted in a shielded chamber on six healthy subjects from 28 to 42 years old. Two series of 30-day experiments were performed, in each of which three persons participated simultaneously. The daily cyclogram of the activity of subjects in both series foresaw three strictly regulated 24-hour "sleep-wakefulness" schedules, organized in such a way as to insure that at any one time, one of the experiment's participants would be serving an 8-hour watch. One of the employed schedules required the subject to be awake from 1000 to 0200 hours and asleep from 0200 to 1000 hours; the second required wakefulness from 0200 to 1800 hours and sleep from 1800 to 0200 hours, and the third required wakefulness from 1800 to 1000 hours and sleep from 1000 to 1800 hours. In one of the stages of the experiment each subject had to serve a continuous watch for 64 (first series) and 72 hours (second series).

The continuous watch was planned on the 3d day in the first daily schedule, on the 13th day in the second, and on the 23d in the third.

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Sleep dynamics were subjected to integrated study: EEG data (one night every 4-5 days) recorded with right and left frontal-occipital points of contact, continuously throughout the night, with a 17-channel electroencephalograph manufactured by the "Saney-Instrument" company; motor activity (actograms) recorded daily on a special actograph with direct-contact sensors, continuously during each night; subjective assessment of sleep by the subject (analysis of questionnaires filled out daily).

Analysis of EEG's required consideration of the nature of the dominating rhythms and their magnitude (frequency, amplitude, and index), which were used to determine the EEG stages (4, 8), their duration, and their succession throughout the night. In doubtful cases the EEG stages were determined with the help of oculograms (eye movements recorded on the EEG) and the motor activity data. The actogram data were used to evaluate the percentage of calm 5-minute intervals and the number of movements per hour of sleep. The adequacy of sleep was determined subjectively, as were the self-assessments of subject health.

Research Results and Their Discussion

In the first series of experiments the sleep dynamics of the subjects were studied using the same daily activity schedule in all stages. As follows from the obtained data, subject F-v, who followed a schedule calling for a slight shift in cycles, exhibited sleep characteristics hardly differing from normal within just 3 days (Figure 1, *Ia*, Table 1, *a*, Table 2, 1). His time for falling asleep did not exceed 5-10 minutes during this period. The EEG was dominated by deep slow-wave and paradoxical stages. Motor activity was low throughout the night (2.8 movements per hour), though the subject subjectively described the quality of his sleep as fully adequate. Immediately after 64 hours of uninterrupted wakefulness (Figure 1, *Ib*, Table 1, *b*, Table 2, 2) the subject's sleep became even deeper, as is evidenced by the short time required to fall asleep (1-2 minutes), the low motor activity (1.9 movements per hour), and the dominance of deep slow-wave stages in the EEG. In the following days, the 8th-13th (Figure 1, *Ic*, Table 1, *c*, Table 2, 3, 4), the sleep indicators deteriorated insignificantly, and then they persisted at one level (Figure 1, *Ie*, Table 1, *d*, *e*; Table 2, 5-8), which indicates relative completeness of the subject's retuning to the new "sleep-wakefulness" schedule.

Sleep disturbances were more significant in the first days for subject S-vka, who followed a schedule with a 6-hour shift in cycles (Figure 1, *IIa*, Table 1, *f*, Table 2, 1). He required from 30 to 80 minutes to fall asleep, and his sleep was intermittent, especially in the first half of the night, exhibiting a relative increase in the superficial slow-wave stages of the EEG and heightened motor activity (7.3 movements per hour). The sleep dynamics improved by the 7th-12th days, though insignificantly (Figure 1, *IIc*, Table 1, *g*, *h*, Table 2, 3). The time for falling asleep averaged 40-50 minutes, motor activity was relatively high (5.7 movements per hour), and growth in the superficial slow-wave stages was observed in the EEG. Immediately following 64 hours of continuous wakefulness (Figure 1, *IId*, Table 1, 4, Table 2, 4) the subject's sleep became continuous. He fell asleep quickly, the proportion of deep slow-wave EEG stages increased, and motor activity was low (2.4 movements per hour). In the next 3 days the sleep dynamics deteriorated somewhat, but they were better in terms of the EEG stages and motor activity (Figure 1, *IIe*, Table 1, *j*, Table 2, 5) than prior to the period of continuous wakefulness.

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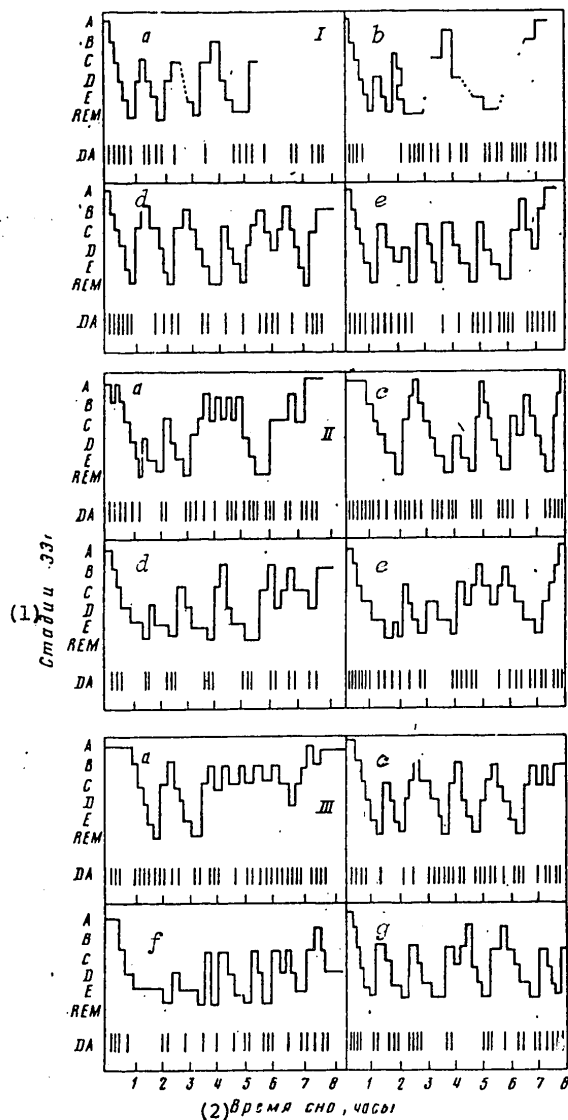


Figure 1. Dynamics of EEG Stages and Motor Activity of Three Subjects During Sleep (First Series): I--subject F-v (sleep from 0200 to 1000 hours), II--subject S-vka (sleep from 1800 to 0200 hours), III--subject B-sh (sleep from 1000 to 1800 hours), a--3d day, b--7th day, c--12th day, d--15th day, e--23d day, f--27th day; A, B, C, D, E, REM--EEG stages; DA--motor activity

Key:

1. EEG stages

2. Time of sleep, hours

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Table 1. Duration of EEG Stages During the Sleep of Subjects Following Schedules Lacking Change in "Sleep-Wakefulness" Cycles, % (First Series)

(1) Грабли ээг	(2) Испытуемый Ф-в (сон с 2 до 4 ч)					(3) Испытуемый (3) (сон с 18 до 2 ч)								(4) Испытуемый Б-ш (сон с 10 до 18 ч)							
	3 сут. а	7 сут. б	13 сут. в	20 сут. г	29 сут. д	3 сут. е	7 сут. ж	12 сут. з	15 сут. и	19 сут. к	24 сут. л	28 сут. м	3 сут. н	7 сут. о	12 сут. п	23 сут. р	28 сут. с				
	а	б	в	г	д	е	ж	з	и	к	л	м	н	о	п	р	с				
A	6,4	4,8	8,3	4,0	14,6	4,9	6,4	9,7	1,9	6,3	7,0	4,9	19,1	12,5	4,3	4,7	4,0	4,1			
B	12,8	4,8	12,5	14,0	6,2	19,6	10,6	17,1	16,0	6,3	10,3	7,3	30,0	12,5	18,1	6,5	6,0	8,2			
C	22,5	23,8	25,0	40,0	28,3	29,8	21,3	19,5	20,4	23,4	17,0	17,1	34,0	20,0	30,0	23,8	22,0	20,4			
D	16,1	19,0	20,8	18,0	16,6	12,0	14,9	17,1	16,0	21,3	20,7	12,2	6,4	12,5	17,0	23,8	22,0	14,3			
E	22,5	33,3	16,7	8,0	17,6	17,0	21,3	21,9	30,6	27,7	20,7	34,1	6,4	27,5	14,8	23,8	30,0	30,6			
REM	19,7	14,3	16,7	16,0	16,7	16,7	25,5	14,7	15,1	15,0	24,3	24,4	4,1	15,0	15,8	17,4	16,0	22,4			

*1st day following 72 hours of continuous wakefulness.

Key:

1. EEG stages
2. Subject F-v (sleep from 0200 to 0400 hours)
3. Subject S-vka (sleep from 1800 to 0200 hours)
4. Subject B-sh (sleep from 1000 to 1800 hours)
5. Day

Beginning with the 19th-20th days the sleep indicators once again improved somewhat (Figure 1, IIe, Table 1, k, l, Table 2, 8). Although it took him 20-30 minutes to fall asleep during this period of time, his sleep was deep, and it exhibited a typical distribution of orthodox and paradoxical sleep, and motor activity was low (6.0 movements per hour).

Distinct sleep disturbances were observed for subject B-sh, who followed a schedule with an 11-hour shift in cycles. As follows from the data in Figure 1, IIIa-g Table 1, m-p, and Table 2, for a long period of time this subject's sleep was intermittent and superficial, lasting not more than 5 hours. His sleep disturbances were most pronounced in the first 3-5 days. During these days he needed from 30 to 60 minutes to fall asleep. Superficial slow-wave stages were represented to a greater extent in the EEG, and motor activity was considerably high (8.4 movements per hour). According to subjective assessments, sleep was inadequate for restoration of work efficiency. As the subject accustomed himself to the new schedule, the sleep dynamics gradually improved in both the qualitative and quantitative respects, attaining a stable level by the 16th-20th days (Figure 1, IIIe, Table 1, p, Table 2, 5). In this period the subject required an average of 10-15 minutes to fall asleep. A typical distribution of stages of orthodox and paradoxical sleep were observed in the EEG, motor activity was low (5.1 movements per hour), and according to the subjective assessments by the subjects, sleep was fully adequate. Immediately after 64 hours of continuous wakefulness (Figure 1, IIIf, Table 1, a, Table 2, 7) the subject's sleep was deep, he fell asleep quickly, his motor activity was low (1.9 movements per hour), and total sleeping time was about 8 hours. In the following days the sleep dynamics decreased somewhat (Figure 1, IIIg, Table 1, r, Table 2, 8), but in relation to the basic components (falling asleep time, depth, duration) they were the same as immediately before the time of continuous wakefulness.

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Table 2. Dynamics of Motor Activity Indicators for Sleeping Subjects (Average Data)

(1) Серия	(2) Испыту- емый	(3) Показатели	1-3 сут. (1)	4-7 сут. (2)	8-11 сут. (3)	12-15 сут. (4)	16-19 сут. (5)	20-23 сут. (6)	24-27 сут. (7)	28-30 сут. (8)
(5)	Ф-в	ПСП	72,2	86,6	74,0	74,0	73,8	70,0	79,6	74,2
		ДА	2,8	*1,9	3,6	3,1	3,6	4,1	3,5	4,3
{6}	С-вка	ПСП	59,3	63,6	65,7	80,1	66,0	63,2	64,0	71,3
		ДА	7,3	5,6	5,7	*2,4	4,9	5,6	6,6	5,9
(7)	Б-ш	ПСП	60,7	60,5	56,0	60,8	61,2	58,5	84,2	61,1
		ДА	6,4	5,4	5,6	5,3	5,1	5,7	*1,9	5,7
(8)	Х-в	ПСП	57,6	58,3	41,7	38,5	52,1	61,5	58,3	47,9
		ДА	5,8	*5,9	10,1	12,1	8,1	6,5	7,4	10,4
II (9)	С-к	ПСП	59,1	55,4	65,0	69,8	64,6	67,7	56,3	52,6
		ДА	6,4	5,0	5,4	*4,2	6,5	5,0	10,0	9,6
(10)	С-н	ПСП	51,3	61,5	50,0	44,8	48,9	61,5	70,0	62,5
		ДА	6,7	7,0	11,4	10,0	8,8	7,3	*5,0	7,3

*1st day following prolonged continuous wakefulness; ПСП--percentage of calm, 5-minute intervals, nightly average; ДА--number of movements per hour, nightly average.

Key:

- | | |
|---------------|----------|
| 1. Series | 6. S-vka |
| 2. Subjects | 7. B-sh |
| 3. Indicators | 8. Kh-v |
| 4. Days | 9. C-k |
| 5. F-v | 10. S-n |

Thus we can distinguish three stages in the first series in terms of the nature of sleep dynamics. The first was typified by worsening of the sleep indicators of all subjects for several days and subsequent recovery of sleep; the causes of this were, on one hand, transition to a new schedule (3, 6, 9-11) and, on the other hand, the influence of the unusual conditions of the isolated space (1, 9, 12). In this case while the shift in cycles was small (sleep from 0200 to 1000 hours), the sleep disturbances were slight, and sleep recovery required a few days. With 6-hour (sleep from 1800 to 0200 hours) and 11-hour (sleep from 1000 to 1800 hours) shifts in the cycles, the sleep disturbances were more pronounced, and sleep recovery dragged on for up to 2-3 weeks. In this respect the obtained data are consistent with the results of my previous research (9, 10) and the research data of other authors (3, 11, 13). A 64-hour period of continuous wakefulness (the second stage) promoted a short-term increase in the duration of sleep and an improvement in its qualitative characteristics in terms of all parameters, though predominantly due to growth in the proportion of deep slow-wave stages, noted in works (14-17). Following the period of continuous wakefulness (the third stage), changes in sleep dynamics were practically insignificant, which indicated completion of this function's retuning to the new schedule of daily activity.

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Somewhat different features were observed in sleep in the second series of experiments, in which each subject followed from two to three daily activity schedules in connection with a 72-hour period of continuous wakefulness. As follows from the experimental data, the sleep indicator for subject Kh-v, who initially followed a schedule with a small shift in cycles (sleep from 0200 to 1000 hours), hardly differed from normal by the 3d day (Figure 2, *Ia*, Table 3, *a*, Table 2, *1*). The time he required to fall asleep during this period was 5-10 minutes. The EEG was dominated by deep slow-wave and paradoxical stages, and motor activity was low (5.0 movements per hour). According to subjective data, sleep was adequate.

In the 1st day following 72 hours of continuous wakefulness, despite maintenance of a new schedule (sleep from 1000 to 1800 hours) the sleep of the subject was the same as in the previous series--it was deep, the subject fell asleep quickly, his motor activity was low (Figure 2, *Ib*, Table 3, *b*, Table 2, *2*), and sleep duration was about 8 hours. In subsequent days (Figure 2, *Ic*, Table 3, *c*, Table 2, *3-5*) the sleep dynamics were disturbed in both qualitative and quantitative respects. The time the subject required for falling asleep increased dramatically (to 25 minutes), sleep became intermittent, the EEG was dominated by superficial slow-wave stages, and motor activity was high (up to 12.0 movements per hour). The total time of sleep dropped to 3.5-4.5 hours, and according to the subject's subjective assessment, his sleep was inadequate for restoration of work efficiency. By approximately the 15th-20th days (Figure 2, *If*, Table 3, *e*, Table 2, *6*) the duration of sleep increased somewhat, reaching 5.5-6.5 hours, but its quality remained poor until the end of the experiment, which obviously indicates that this subject had difficulties in adapting to the new "sleep-wakefulness" schedule.

Table 3. Duration of EEG Stages During Sleep of Subjects Following Schedules Involving a Shift in "Sleep-Wakefulness" Cycle, % (Second Series)

(1) Субъект ЭЭГ	(2) Испытуемый Х-в						(3) Испытуемый С-к						(4) Испытуемый С-н					
	5 сут.		10 сут.		15 сут.		7 сут.		12 сут.		15 сут.		2 сут.		8 сут.		21 сут.	
	г	д	г	д	г	д	г	д	г	д	г	д	г	д	г	д	г	д
A	9,5	4,6	32,8	33,3	28,0	4,3	6,0	13,6	6,8	8,0	22,8	7,5	40,0	4,4	20,4	2,1		
B	15,8	16,3	19,5	13,9	11,6	14,9	12,7	22,7	15,9	8,9	14,6	30,0	8,6	12,6	24,5	2,1		
C	23,8	16,3	10,8	30,5	18,6	23,4	31,2	31,7	22,7	27,2	20,8	40,0	20,0	27,7	18,3	20,9		
D	14,3	20,9	10,8	10,1	14,0	21,3	18,7	22,7	15,7	14,7	12,5	10,0	11,4	17,0	8,2	14,0		
E	17,5	25,6	15,3	5,1	16,2	19,1	18,7	4,8	20,5	14,7	16,8	5,0	14,3	21,3	14,3	40,0		
REM	19,1	16,3	10,8	7,1	11,6	17,0	12,7	4,7	18,4	26,5	12,5	7,5	5,7	17,0	14,3	20,9		

*1st day following 64 hours of continuous wakefulness; first schedule (sleep from 0200 to 1000 hours)--*a, j, k, l, n*; second schedule (sleep from 1800 to 0200 hours)--*g, h, i, o, p*; third schedule (sleep from 1000 to 1800 hours), *b, c, d, e, f, m*.

Key:

1. EEG stages
2. Subject Kh-v
3. Subject S-k
4. Subject S-n
5. Day

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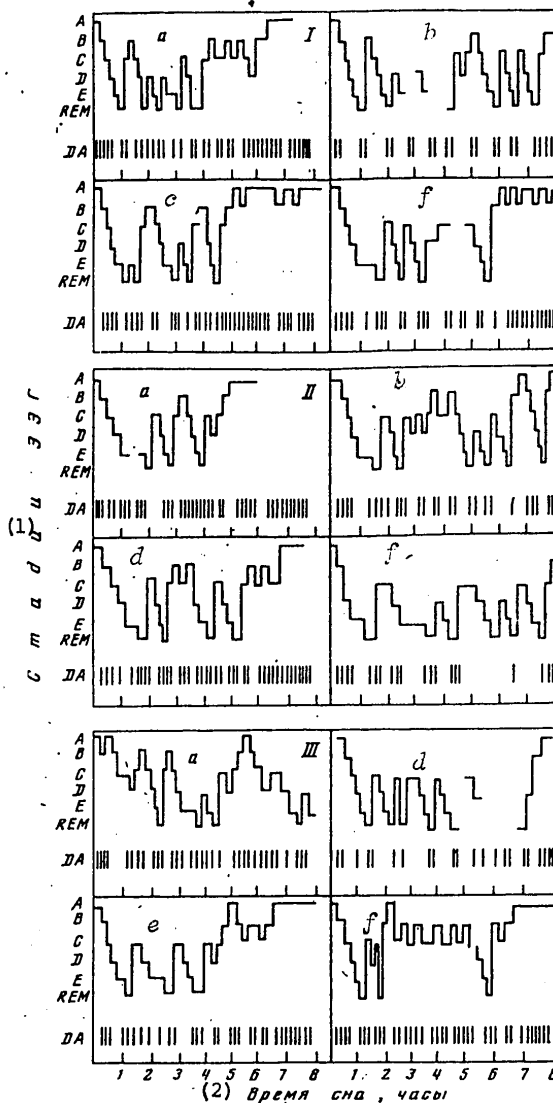


Figure 2. Dynamics of EEG Stages and Motor Activity of Three Subjects During Sleep (Second Series): I--subject Kh-v (sleep from 0200 to 1000 hours--a; sleep from 1000 to 1800 hours--b, c, f), II--subject S-k (sleep from 1800 to 0200 hours--a,b; sleep from 0200 to 1000 hours--d,f); III--subject S-n (sleep from 1000 to 1800 hours--a; sleep from 0200 to 1000 hours--d; sleep from 1800 to 0200 hours--e,f). See Figure 1 for other symbols.

Key:

1. EEG stages
2. Time of sleep, hours

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Rather distinct sleep disturbances were noted for subject S-k, who initially followed a schedule with a 6-hour shift in cycles. As can be seen from the obtained data, this subject's sleep was clearly inadequate for several days (Figure 2, *IIa*, Table 3, *g*, Table 2, *1*). It was hard for him to fall asleep, he woke up frequently, his motor activity was high, and total sleeping time was about 5-6 hours. By the 7th-12th days, as in the first series with a similar schedule, the sleep dynamics improved somewhat, duration attaining 7-7.5 hours (Table 3, *c*, Table 2, *3*). The time required for falling asleep during this period was 20-30 minutes, the ratio between deep slow-wave and paradoxical sleep stages increased, motor activity dropped (to 5.0 movements per hour), and according to subjective assessments of the subject, sleep appeared fully adequate. Immediately after 72 hours of continuous wakefulness (Figure 2, *II d*, Table 3, *j*, Table 2, *4*), subject S-k's sleep improved significantly in both quantitative and qualitative respects despite transition to a new schedule (sleep from 0200 to 1000 hours), as was evidenced by the time required to fall asleep (2-5 minutes), the low motor activity (4.2 movements per hour), and significant growth in the proportion of deep slow-wave stages in the EEG. Sleep worsened in subsequent days despite a schedule with just a slight shift in cycles (Figure 2, *II e*, *f*, Table 3, *k*, *l*, Table 2, *5-8*). It subsequently remained at the lower level until the end of the experiment.

Sleep disturbances were found to be even more pronounced for subject S-n, who followed a schedule calling for frequent shifts in the "sleep-wakefulness" cycles. As follows from the obtained data (Figure 2, *III a*, Table 3, *m*, Table 2, *1*), in the first 3 days, in which the subject followed a schedule with an 11-hour shift in sleep cycles, sleep was intermittent, with frequent awakenings and high motor activity (up to 7.0 movements per hour), similarly as with subject B-Sh in the first series. After the subject switched to a schedule with a 3-hour shift in cycles (Figure 2, *III b*, Table 3, *n*, Table 2, *3*), the sleep indicators improved somewhat. The time required for falling asleep decreased to 5 minutes. The EEG was dominated by deep slow-wave and paradoxical sleep, and sleep duration increased. After transition, in the 13th through 15th days, to a schedule calling for a 6-hour shift in cycles (Figure 2, *III d*, Table 3, *o*, Table 2, *4*), sleep dynamics deteriorated once again. During this period the time the subject needed to fall asleep increased dramatically (up to 40 minutes), sleep became intermittent with a low proportion of deep slow-wave and paradoxical sleep, motor activity became high (up to 10 movements per hour), and total sleep duration did not exceed 3.5-4.5 hours. In the first days following 72 hours of continuous wakefulness the sleep indicators deteriorated dramatically, as with the other subjects (Figure 2, *III f*, Table 3, *p*, Table 2, *7*). Sleep during this period was typified by a short time for falling asleep, low motor activity, and a dramatic increase in the proportion of deep slow-wave stages. In subsequent days the subject's sleep indicators once again deteriorated, though insignificantly, the time required for falling asleep increased (up to 50 minutes), motor activity grew (7.3 movements per hour), the quantity of superficial slow-wave stages increased, and according to subjective assessments, sleep became inadequate.

Thus as with the first series, in this series we can distinguish three stages in the sleep dynamics of the subjects. The first (prior to continuous wakefulness) was typified first by a worsening of sleep and then by its improvement, reflecting a certain amount of influence of isolation and an altered work-rest schedule (9, 10, 18, 19). Only for one subject, who followed three different schedules in the first

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stage, were the sleep indicators significantly worse with each transition, obviously due to insufficient retuning of this function by the moment the daily activity schedule was changed again. A period of 72 hours of continuous wakefulness (the second stage) promoted significant improvement in the qualitative characteristics of the sleep of all subjects (predominantly due to small-wave stages), and an increase in sleep duration, despite assumption of a new work-rest schedule. In subsequent days (the third stage) sleep once again deteriorated significantly, remaining at a low level for a long period of time, indicating greater difficulty experienced by the subject in adaptation to the new daily activity schedule immediately following prolonged sleep deprivation.

Conclusions

1. Man's adaptation to a new daily activity schedule is closely associated with the degree to which the "sleep-wakefulness" cycles are shifted. When the cycles were shifted to just a slight degree, the sleep disturbances of the subjects were less pronounced, and subsequent sleep recovery occurred more quickly. An increase in the extent of cycle shift led to growth in sleep disturbances, and subsequent lengthening of sleep restoration time.
2. Frequent change in the "sleep-wakefulness" schedule, occurring every 5-7 days, led to more-pronounced sleep disturbances and longer adaptation, which indicates the significance of the time factor (realization of the principle of successive and selective reaction) in man's adaptation to an altered daily schedule.
3. Prolonged continuous wakefulness caused significant improvement in the quantitative and qualitative characteristics of sleep in all subjects, irrespective of the nature of the schedule followed and the degree of adaptation to it. However, this improvement was predominantly the result of growth in the proportion of deep slow-wave stages. In subsequent days the changes in sleep dynamics were closely associated with the nature of the schedule followed and the time for which it was followed: When the same schedule was employed (first series) the sleep indicators hardly changed at all; when a new schedule was assumed (second series) significant sleep desynchronization was observed, coupled with pronounced lengthening of the restoration time, apparently caused by the asthenic influence of prolonged sleep deprivation.
4. The combination of altered schedules and sleep deprivation causes even more-pronounced disturbances of psychophysiological state and the individual's work efficiency, than was the case in similar conditions without sleep deprivation (10, 18, 19). In this case the obtained data may be useful in development of daily cyclograms for the activity of operators doing stressful work in isolated spaces, and in prediction of the functional capabilities in such conditions.

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